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# **STRESS AND SLEEP: PREVALENCE, VULNERABILITY AND DAY-TO-DAY VARIATION**

Helena Petersen



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Stress and sleep: prevalence, vulnerability and day-to-day variation  
THESIS FOR DOCTORAL DEGREE (Ph.D.)

By

**Helena Petersen**

*Principal Supervisor:*

Professor Torbjörn Åkerstedt  
Karolinska Institutet  
Department of Clinical Neuroscience  
Division of Psychology

*Co-supervisor(s):*

Professor Göran Kecklund  
Stockholm University  
Department of Psychology  
Division of Stress Research Institute

Professor John Axelsson  
Stockholm University  
Department of Psychology  
Division of Stress Research Institute

*Opponent:*

Associate Professor Jan-Erik Broman  
Uppsala University  
Department of Neuroscience  
Division of Psychiatry

*Examination Board:*

Associate Professor Christian Benedict  
Uppsala University  
Department of Neuroscience  
Division of Functional Pharmacology

Associate Professor Aila Collins  
Karolinska Institutet  
Department of Clinical Neuroscience  
Division of Psychology

Professor Peter Johansson  
Linköping University  
Department of Health, Medicine and Caring  
Sciences  
Division of Nursing Sciences and Reproductive  
Health



To Dante and Michelle for turning every day into an unexpected adventure.



## ABSTRACT

Stress and sleep problems are increasingly common in society with consequences not only for individual health, but also high societal costs. The focus of this thesis is how sleep is affected by day-to-day variation in naturally occurring stress, the impact of individual vulnerability to stress-related sleep disturbances and the causes people attribute their disturbed sleep to. This was investigated through polysomnographically (PSG) recorded sleep in home-settings during periods of different levels of work stress, sleep diaries over extended periods and a population-based survey on prevalence and association of stress and disturbed sleep.

The results suggest that moderate intensity, short-term stress has a limited negative impact on sleep, in terms of a decreased sleep efficiency and self-rated non-restorative sleep. However, the response was stronger in individuals with a pre-existing trait of vulnerability to stress induced sleep disturbances, resulting in a more fragmented sleep and decreased duration of rapid eye movement (REM) sleep. Although the day-to-day variation in sleep quality appeared to be quite sensitive to small variations in stress level, a key factor seemed to be the presence of stressful thoughts and worries at bedtime.

The weekend appeared to serve as a possibility to compensate the sleep impairment of the workweek, as sleep duration was extended and the amount of slow wave sleep (SWS) increased. In chronically stressed individuals in the general population however, sleep duration was not compensated, instead a reduction was seen for both weekdays and weekend, suggesting an impaired recovery ability related to a high frequency of stress.

The general population, particularly the women and persons in the younger age-groups, most commonly attributed their sleep problems to stress. The highest prevalence of stress was seen in the 35-44 age group, while the peak for prevalence of stress disturbed sleep occurred a little later, in the age 45-54 years.

It was concluded that the most common attribution of poor sleep is stress, and that everyday stress had a negative effect on polysomnography, but at a rather modest level, although the effect was larger on those reporting a pre-existing sleep sensitivity to stress.

*Key words: sleep, stress, polysomnography, recovery, sleep diary, population-based.*

## LIST OF SCIENTIFIC PAPERS

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- III. Åkerstedt, T., Orsini, N., Petersen, H., Axelsson, J., Lekander, M. & Kecklund, G. (2012). Predicting sleep quality from stress and prior sleep – A study of day-to-day covariation across six weeks. *Sleep Medicine*, 13(6): p. 674-679.
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## LIST OF ABBREVIATIONS

|          |                                       |
|----------|---------------------------------------|
| ACTH     | Adrenocorticotrophic hormone          |
| ANOVA    | Analysis of variance                  |
| ANS      | The autonomic nervous system          |
| CNS      | The central nervous system            |
| CRH      | Corticotropin-releasing hormone       |
| ECG      | Electrocardiography                   |
| EEG      | Electroencephalography                |
| EMG      | Electromyography                      |
| EOG      | Electrooculography                    |
| FIRST    | Ford Insomnia Response to Stress Test |
| HADS     | Hospital Anxiety and Depression Scale |
| HPA axis | Hypothalamic-pituitary-adrenal axis   |
| KSD      | Karolinska Sleep Diary                |
| KSS      | Karolinska Sleepiness Scale           |
| KSQ      | Karolinska Sleep Questionnaire        |
| NREM     | Non-rapid eye movement sleep          |
| PSG      | Polysomnography                       |
| PSNS     | Parasympathetic nervous system        |
| REM      | Rapid eye movement sleep              |
| SAM axis | Sympathetic-adrenal-medullary axis    |
| SE       | Sleep efficiency                      |
| SL       | Sleep latency                         |
| SMBQ     | Shirom-Melamed Burnout Questionnaire  |
| SNS      | Sympathetic nervous system            |
| SQI      | Sleep quality index                   |
| SWS      | Slow wave sleep                       |
| TST      | Total sleep time                      |
| WASO     | Wake after sleep onset                |



# 1 INTRODUCTION

This thesis is an effort to understand more about the relationship between stress and sleep. In particular, the effect of that, often seemingly unavoidable, moderate stress in day to day life that many people experience.

My interest in stress and sleep stems very much from personal experiences. While studying for my bachelor degree, I also simultaneously worked a fulltime nightshift in a nursing home which eventually resulted in burnout. That inspired me to pursue a master's degree in stress prevention which was how I ended up at the Stress Research Institute (IPM at that time). During my early PhD studies, I was diagnosed with swine-flu related hypersomnia and these experiences combined with my education led me to believe I knew better than most people what it meant to be stressed and sleepy in the worst possible way. But now, as I'm writing this thesis in the midst of the corona-pandemic, with a 2-year old and a 3-year old child at home, and I can honestly say that I have never been more wrong about anything in my life. Stress has become the norm and a full night's sleep is now the ultimate dream. With that said, if I had the choice to go back to my former relatively stress free, less sleep deprived life without children and thesis writing, of course I choose my present life (although corona I could do without). That is in a sense what this thesis is about, the everyday, normal life stress and disturbed sleep we cannot (or will not) avoid, and the effect it may have on us, and on our sleep quality in particular.



## 2 BACKGROUND

### 2.1 STRESS

Stress is a subject well known to most people; we constantly hear about increased stress due to demands of the 24/7 society we live in. In Europe, as much as a quarter of employees report work-related stress (Vargas, Flintrop et al. 2014). Data from the 2018 national public health survey (Folkhälsomyndigheten 2018) (The Public Health Agency of Sweden) estimated that 16 % of the population (women: 19%, men: 12 %) had experienced some degree of stress, and 4 % a very high degree of stress over the last two weeks. The prevalence of stress is however difficult to compare between different surveys and with other countries because of sample characteristics, different measures of stress being used (Cohen, Kessler et al. 1997) and difference in interpretation of stress across cultures and even on an individual level. Almeida et al (2002) examined a US national sample using telephone interviews and found that people experienced some form of stressor on average 3 days per week and multiple stressors 0.8 days/week (Almeida, Wethington et al. 2002). In a British national survey, 82% of the sample reported that they during a typical week felt stressed at least some time, while only 8% felt stressed all the time (AXA 2017). So even if an absolute prevalence is hard to obtain, the examples above gives us an idea of how prevalent stress is and paints a somewhat gloomy picture. It seems almost everybody nowadays complain about being stressed and “know” that stress is bad for them and for their sleep. Being a subjective experience as well as a physiological phenomenon, people are allowed to interpret it however they like. But for the purpose of coherency I will begin this thesis by describing what “being stressed” and “sleeping poorly” means in the context of included studies, starting with a brief overview of the theoretical framework stress and its effects are commonly studied within.

The concept of stress is very wide and not the easiest one to define, particularly since stress does not only mean one thing. It describes both the stimulus (stressor), the subjective experience of the stressor, the physiological response to the stressor and the experience of that response. Stress is also highly individual, what stresses one person out completely may be uplifting and stimulating for another depending on personality, social support, coping strategies and other factors.

In physics, the word stress is used to describe the interaction between a force and the counter resistance to that force. Hans Selye is known as the father of stress research and was the first to incorporate the physics term stress into medicine (Selye 1950). He defined stress as an automatic reaction to an external stressor, i.e. a state of physical arousal to meet demands encountered by the organism. As a biological function, stress in itself is by no means designed to be dangerous. On the contrary, it is a survival drive meant to increase our ability to get through or get away from threatening situations, for instance by freeing and re-distributing energy and increase blood pressure and cardiac output, providing more blood to skeletal muscles in order to help us run faster. Other effects of the stress response that are useful when facing danger is improved alertness, attention and focus, and enhanced ability to remember important aspects of the threatening situation (McEwen 2000) (Olsson 1999)

(Chajut and Algom 2003). This enhanced cognitive ability however requires that the intensity of stress is at just the right level (for that particular individual) (Chrousos and Gold 1992). When the high tonic activation that helps us in the short-run is sustained, stress may very well become harmful instead (Cooper 2005) (McEwen 2004). The problem arises when we are facing other types of threats than the stress system was designed for, which is mainly involving intense physical activity and being of an acute and short timeframe. Evolution has us nowadays more commonly facing on-going, medium intensity stress at work as opposed to running from predators (McEwen and Stellar 1993) (McEwen 2004).

It may sound like the stress system is merely an ancient function from the time of sabre-toothed tigers but that is a far from accurate description. Getting us physically prepared to meet danger may be the main function, but the stress system is intricately involved in our daily life in many other ways as well, like keeping us awake during the day and adjusting the blood pressure according to body position for example. Before I go into the biological functions of the systems involved in the stress response in more detail, the following paragraphs concerns stress as a theoretical concept. It has been viewed from purely physical standpoints, behavioral, psychological, and all kinds of combinations. A comprehensive summary and comparison of all definitions and theories of stress that have been put forward since the start of stress research can be found elsewhere, I only aim to cover some of the most central ones, of relevance to this thesis.

### **2.1.1 Theories of stress**

One of the earliest theories of stress was Walter Cannon's Fight or flight response (Cannon 1914) (Cannon 1915). According to his theory, perceived threats causes animals to react with a general activation of the sympathetic nervous system in purpose of preparing the animal to either fighting the threat or fleeing from it (Jansen, Nguyen et al. 1995). This reaction is equivalent to the modern term hyperarousal or acute stress response. Based on the underlying concept of evolution, Cannon viewed the fight or flight response as a survival instinct designed to keep us alive. Individuals with strong instincts to react swiftly by either running away from danger or fight for their lives would have the highest chance of survival and thus these genetic traits would continue to be strengthened over generations. Fight and flight represent the choices we have when confronted with potential danger, but later it was observed that certain animal species reacted to danger by playing dead, and a third strategy, freeze, has been suggested as a common behavioral stress response also in humans (Tyhurst 1951, Arnsten, Mazure et al. 2012). The theory has by some researchers been critiqued for predominately being based on studies of men, as differences between genders have been found in stress reactions. While men mostly react with fight, women more frequently freeze or flee (Taylor, Klein et al. 2000). The fight-or-flight response is today recognized as part of the first stage of Hans Selye's stress theory, "The General Adaptation Syndrome" (Selye 1950). Within this model Selye described stress as a "nonspecific response of the body to any demand". The non-specific physiological response consists of three stages, alarm, resistance and exhaustion. During the alarm stage the body adjusts to meet the demands by secreting



corticosteroids, and during resistance the adaptation to the stressor takes place. According to Selye, if the stress is prolonged, the organism is no longer able to adapt to meet the demands of the stressor, i.e. secrete sufficient amounts of corticosteroids, which would lead to exhaustion and could contribute to disease (Selye 1946) (Selye 1956).

As mentioned earlier, the stress response is not all bad, it is actually meant to protect us, and stress mediators like cortisol and catecholamines indeed have positive as well as damaging effects. McEwen and Stellar (1993) found the term “stress” contradictory in this sense and formulated a new way of describing the relationship between stress and illness (McEwen and Stellar 1993) (McEwen 1998). They recycled the term allostasis, originally used by Sterling and Eyer (1988) to describe the adjustments of the cardiovascular system (Sterling and Eyer 1988), applying it to other physiological mediators like stress hormones. The literal meaning of the term is "maintaining stability (or homeostasis) through change", and in this context it refers to the short-term alterations of the physiological systems in the body necessary to adapt to challenges. The term allostatic load describes the cumulative ‘wear and tear’ the body is subjected to from repeated activation of the stress system, i.e. allostasis (McEwen 1998). Every system in the body have both immediate protective adaptive actions (allostasis) and long-term potentially damaging effects (allostatic load). One example of this is the secretion of catecholamines for adjusting heart rate and blood pressure for various functions. If the blood pressure is upregulated over and over again due to work stress or the system fails to shut down when the perceived challenge is over it could lead to atherosclerosis and other health risks. The cumulative cost of longer periods of stress, combined with genetics, previous experiences and developmental factors predisposes the effect of acute stressful events. This allows for significant individual differences in susceptibility to stress and disease, and in what we initially perceive to be stressful.

Lazarus’ and Folkman’s transactional model of stress and coping views stress as being the result of an individual being unable to, or having insufficient resources available to cope with demands (Lazarus and Folkman 1984). Its neither the stressor or the stress response that is in focus, but rather the appraisal of the stress/stressor. That is, how threatening the individual perceives a specific event, situation or environment to be, will determine both the stress response and how it is managed. The concept of coping is an integral part of the theory, described as the cognitive and behavioral efforts a person uses to handle stress. These strategies are highly individual and constantly changing, meaning everybody handles stress differently and the same person won’t necessarily use the same way of coping if encountering a specific stressor on more than one occasion. According to the theory there are 8 ways of responding to stress, ranging from distancing and avoidance to confrontation and radical acceptance, but common for these are that they are all emotion- or problem focused.

“The Cognitive Activation Theory of Stress” (Ursin and Eriksen 2004) is also a model with focus on coping. The theory attempts to formalize and operationalize the concepts of stress and coping. Stress is seen as a process and the stress response as a natural and necessary physiological response to any imbalance or threat to homeostasis, unpleasant as it may be, it

is not harmful. If the stress response is sustained over time it may however result in illness. The nature of the stress response is dependent on how the individual evaluates the consequences of the stressor and what resources for coping is available. For instance, if the outcome is expected to be positive and the coping fails to achieve this, the result could be feelings of hopelessness.

A stress reaction doesn't necessarily only occur in the presence of a real or imagined threat, many times the body responds in anticipation of, or following, such a situation. These types of anticipatory responses can be conscious or subconscious (Brosschot, Verkuil et al. 2010), and are generated centrally by either conditioning or by an innate predisposition to recognize danger (Herman, Figueiredo et al. 2003). Common phobias like being afraid of snakes or heights are salient examples of the latter. Repetitive thoughts concerning stress-related content are proposed as an extension to stress theory since it provides a linking mechanism between stressful experiences, for instance work related, and impaired recovery after work hours (Brosschot, Pieper et al. 2005). Perseverative cognition is defined as "the repeated or chronic activation of the cognitive representation of one or more psychological stressors" (Brosschot, Pieper et al. 2005), i.e. a continuous worrying about past or future negative events. The perseverative cognition hypothesis states that the stress response in itself is often short and is therefore unlikely to cause physiological harm. Instead, it is the continuous worrying about the stressor that links stress to disease by prolonging the stress reaction and increasing the time of "wear and tear" on the body (Brosschot, Pieper et al. 2005). Physical evidence supporting this theory includes for example findings of increased heart rate and elevated cortisol levels associated with perseverative cognition (Ottaviani, Thayer et al. 2016).

A great deal of stress research is devoted to stress and stressors that has to do with employment. The well-established association between stressful psychosocial work characteristics and health problems is mediated by stress-related physiology (Cox and Ferguson 1994). When exposed to job stressors, the stress response system kicks in and activate various physiological reactions such as releasing adrenaline, noradrenaline and elevated blood pressure and cortisol. These reactions are however meant to be acute and should ideally disappear soon after the stress exposure has ceased (Lundberg and Frankenhaeuser 1980). One of the most influential models in work-related stress research is the Job Demand Control Support Model (Karasek and Theorell 1990). Originally it was only focused on job demands and job control (also referred to as decision latitude), and social support was later added as it seems to act as a buffer against the negative effects of high demands (Johnson and Hall 1988). The model postulates that the combination of high job demand and low job control (termed "high-strain job") are negatively associated with both physical and psychological health problems over time (Belkic, Landsbergis et al. 2004) (de Lange, Taris et al. 2003).

Another influential work-stress theory is the Effort-Recovery theory (Meijman and Mulder 1998). The key assumption of the Effort-Recovery theory is that effort expenditure at work is

unavoidable, and this produces load reactions, i.e. stress-related physiological changes. Typically, these reactions will decrease or disappear completely after work hours when the demands cease and some respite is given, that is, the effort needs to be balanced by sufficient recovery. However, under certain circumstances, for example prolonged exposure to high workload without adequate recovery, short term load reactions can accumulate and in the long term lead to development of health problems, including sleep disturbances, fatigue or manifest diseases (van Hooff, Geurts et al. 2005) (Akerstedt 2006) (Sluiter, Frings-Dresen et al. 2001) (Geurts and Sonnentag 2006).

### **2.1.2 Biology of stress**

The stress response involves the entire central nervous system (CNS, i.e. the brain and the brain stem), which is where it all starts. When we are faced with a potentially dangerous situation, an unknown environment, or basically anything that poses a challenge, the brain interprets the event in question, evaluates if it is stressful and consequently initiates the appropriate responses (McEwen 2004). The amygdala, associated with emotional processing, is the area in the brain that does the interpreting. From there a distress signal (given that the object of interpretation was determined to be stressful) is sent out to the hypothalamus, located above the brainstem. The hypothalamus communicates with the rest of the body via the autonomic nervous system (ANS) which regulates involuntary actions in the body such as breathing, heart rate and digestion. The ANS is divided in two parts, the sympathetic nervous system (SNS) and the parasympathetic nervous system (PSNS) (McCorry 2007). If we look at our body as a vehicle, the role of the sympathetic nervous system in the stress response is comparable to being the foot on the gas pedal, stimulating activities that provide energy to the body and optimizes functions needed to “fight or flight”. The parasympathetic nervous system acts sort of like a brake and is responsible for stimulation of “rest and digest” activities in the body, basically keeping the activities of the SNS in check and in so, has the important role of calming the body down after the stress response has served its purpose (Critchley 2005).

After receiving the initial distress signal sent by the amygdala, the hypothalamus activates the SNS. The SNS governs one of the two main axes of the physiological stress response, the sympathetic-adrenal-medullary (SAM) axis (Arnetz and Ekman 2013). The SAM axis is responsible for the immediate actions intended to aid us in either running for our lives or trading punches with the sabre toothed tiger, like increased cardiac output, perspiration, elevated respiratory rate and expanded lung capacity, increased blood flow to skeletal muscles, improved cognitive functions and pupil dilation. These actions are set in motion by signals to the adrenal glands to secrete epinephrine (adrenaline) and norepinephrine (noradrenaline) into the bloodstream. Additionally, epinephrine also triggers stored glucose and fat to be released, ensuring sufficient energy supply. As mentioned above, these actions are immediate, in fact, almost instantaneous which is why it is possible to react to and escape a dangerous situation before fully registering what is happening. As intelligent a species as we may be, evolution acknowledged that we (and most other mammals) wouldn’t survive

that long were we to rely solely on our reasoning of how to behave in dangerous situations, resulting in a system allowing us to make fast adaptations and react to threats (i.e. stressors) quickly and without thought (Mobbs, Hagan et al. 2015) (Darwin 1888).

About 10 seconds later, as a response to signals like the elevated levels of epinephrine and norepinephrine, the hypothalamus activates the other main axis of the stress response, the hypothalamic-pituitary-adrenocortical (HPA) axis, which is governed by the hormonal system and consists of the hypothalamus, the pituitary gland, and the adrenal glands (Folkow 1997). Now corticotropin-releasing hormone (CRH) is secreted into the bloodstream from neurons in the paraventricular nucleus of the hypothalamus. This has two effects, one is increasing the activity of the SNS and thereby perpetuate the effects already put in motion, making sure the foot stays on the gas pedal so to say. The other, and very essential, effect of CRH is that it triggers the secretion of adrenocorticotrophic hormone (ACTH) from the pituitary gland. ACTH finds its way to the adrenal cortex where it stimulates the secretion of glucocorticoid hormones, e.g. cortisol (Mifsud and Reul 2018). Cortisol is instrumental in dealing with stressors lasting beyond a few minutes. It increases gradually and peaks 10–30 minutes into the stress response (Foley and Kirschbaum 2010). Glucocorticoids trigger a sort of emergency mode in the brain that includes various ways of maximizing the energy production, making sure that energy is not wasted on processes deemed non-beneficial in an attack, and ensuring energy is conserved and efficiently supplied during the stress response, for instance by increasing insulin resistance and appetite, restraining inflammation and growth, removing unnecessary cellular components and inactivating non-vital activities (Segerstrom and Miller 2004) (Juszczak and Stankiewicz 2018). When we're being chased by lions or fighting for our lives there is simply no time for the body to prioritize functions and activities like reproduction or going to the bathroom. Once the real or perceived danger has passed, the parasympathetic nervous system takes control and attempts to bring the body back to balance by returning hormonal levels, blood pressure and heart rate to normal. Glucocorticoids are central in terminating the stress response by feedback inhibition of the HPA-axis (McEwen 2000).

All of these processes and intricate chains of actions happening within our bodies are extremely helpful during acute stress and the whole point of it all is to promote homeostasis. Unfortunately, in regard to the physiological stress response, evolution hasn't really been able to keep up with the changes in our environment and the stressors we subject ourselves to. We tend to overreact to stressors that are far from life-threatening, such as impending deadlines at work, traffic jams, relationship drama or even a long line at the supermarket checkout. As the theory of allostasis and allostatic load postulates, too much and too many of the adaptive changes in response to stress can cause dysregulation of the system. Almost all of the adjustments have great short-term effects for the purpose of fighting or fleeing, but when chronically activated they instead may lead to both physical and psychiatric problems (Ketchesin, Stinnett et al. 2017). For instance, overstimulation of the HPA axis and elevated levels of cortisol have been linked to diabetes, obesity and cardiovascular disease (Chrousos 2009), suppressed immune function (Bellavance and Rivest 2014), as well as to mood- and

sleep disorders (Moylan, Maes et al. 2013). Certain cognitive and memory functions are also affected by cortisol secretion (Ennis, Moffat et al. 2016).

### **2.1.3 Burnout**

Burnout is a condition characterized by persistent fatigue and exhaustion that can occur as a result of continuous and long-term stress exposure, especially in connection to stress from psychosocial work factors (Weigelt and Gierer 2019). Other symptoms include physiological exhaustion, emotional distress, cognitive difficulties (e.g. memory and concentration), sleep disturbances and somatic symptoms such as palpitations and muscle pain. In Sweden the official diagnostic term is exhaustion syndrome (Socialstyrelsen 2003), proposed by Åsberg et al (Åsberg, Nygren et al. 2002). The term burnout originated as a psychological phenomenon in healthcare professions and reflected the process of being gradually drained of energy. Freudenberger was the first to define burnout (Freudenberger 1974), originally as a phenomenon exclusively applying to work, but later on expanded to include life in general. There are several definitions of burnout, some view it as a solely psychological construct, while others view it as a combination of psychological and physical exhaustion. The most widespread and influential definition is that of Maslach et.al. (Schaufeli and Enzmann 1998), which describes burnout as a syndrome consisting of emotional exhaustion, depersonalization and reduced personal accomplishment, stemming from work within the service sector, healthcare, education or other people-oriented occupations (Maslach, Jackson et al. 1996) (Maslach 2003). Melamed and colleagues offered another definition, also viewing burnout as a multidimensional construct involving emotional exhaustion, with the addition of physical fatigue and cognitive weariness, together representing the core components of the burnout concept (Melamed, Shirom et al. 2006) (Shirom 1989).

### **2.1.4 Recovery from stress**

Recovery can be defined as a process of psychophysiological unwinding after effort expenditure (Geurts and Sonnentag 2006) or as the time required for the individual's functioning to revert to a pre-stressor level after the imposed stressors are no longer present (Sonnentag and Natter 2004). Factors that may impede recovery by prolonging the physiological activation and possibly result in chronic health impairment are extended exposure to job demands and high workload (Meijman, Mulder et al. 1992) and also cognitive processes such as rumination (Weigelt and Gierer 2019). In particular, the prolonged exposure to job demands can be detrimental to health as continued demands are being made on the psycho-physiological systems already activated during work (Geurts and Sonnentag 2006). When instead an individual is exposed to optimal conditions, that facilitate the recovery process, the resources that have been depleted can be restored (Sonnentag and Zijlstra 2006). Recovery can be passive, meaning a direct release from exposure to job stressors, and also active, for example engaging in social or physical leisure-time activities and may take place both during work hours and on free time out of work (internal and external recovery) (Geurts and Sonnentag 2006). Internal recovery refers to shorter breaks from work and job control while external recovery includes evenings after work hours,

weekends and vacations. Evidence suggests that the daily recovery may be more important for health and well-being than the longer respites (Sonnentag 2001) (Sonnentag 2003), as the positive effects of vacations (Eden 2001) typically fade within a few weeks of returning to work (de Bloom, Kompier et al. 2009). Taking breaks from work can increase productivity and decrease levels of fatigue (Tucker 2003). Further, when the breaks and evening free time are used for restful or stimulating activities as opposed to anything work-related, they have been shown to promote well-being and recovery (Sonnentag and Natter 2004) (Sonnentag and Zijlstra 2006). Activities that are experienced as pleasurable and rewarding can expedite recovery by the increased production of serotonin, beta-endorphins, and other related chemicals that help reverse some of the stress-related physiological reactions (Bodnar 2018). Similarly, physical activities (e.g. sports and exercise) can also promote recovery (Sonnentag, Binnewies et al. 2008) and has been positively related to sleep quality (Banno, Harada et al. 2018).

Sonnentag and Fritz (2007) suggests that which type of activity that are conducive to recovery may differ between individuals and that the psychological processes behind the activities may play an important role. These processes are described as 4 recovery experiences consisting of psychological detachment and relaxation, which promotes recovery through absence of further physiological and psychological demands, while the last two recovery experiences, mastery and control, contribute to recovery by restoring and building up internal resources such as positive mood, skill acquisition and self-efficacy (Sonnentag and Fritz 2007) (Hobfoll and Shirom 2001). Mastery experiences should be challenging but not overtaxing the individual's capabilities (Sonnentag, Binnewies et al. 2008). The experience of control involves the ability to choose how one's time is spent, the activity that is pursued and when, which has been related to lower recovery need, improved sleep quality and health (Sonnentag and Fritz 2007). Engaging in work-related activities during free time has been related to a higher need for recovery (Sonnentag and Zijlstra 2006) and poor well-being at bedtime (Sonnentag 2001). A prolonged exposure to work related stress can lead to a sustained cognitive arousal, for example bedtime worries or rumination, which may hinder the recovery process by impairing sleep and the ability to unwind (Geurts and Sonnentag 2006) (Brosschot, Van Dijk et al. 2007) (Akerstedt, Knutsson et al. 2002). Therefore, the ability to psychologically detach from (i.e. not think about) work during off-work time may be a key factor in stress related sleep disturbances (Akerstedt, Knutsson et al. 2002) (Fahlén, Knutsson et al. 2006). Psychological detachment from work-related issues has been related to many indicators of improved health and well-being, including lower levels of fatigue, decreased need for recovery and less sleep problems (Sonnentag and Bayer 2005) (Brosschot, Gerin et al. 2006) (Sonnentag and Fritz 2007). Conversely, inability to detach from work thoughts during leisure time has proved a strong predictor of sleep problems (Akerstedt, Knutsson et al. 2002) (Cropley, Dijk et al. 2006).

Under normal circumstances (when workload or stress is not extreme), good sleep tend to reduce fatigue and replenish mental resources that have been depleted, thus a vital part of the recovery process (Akerstedt, Nilsson et al. 2009) (Rook and Zijlstra 2006) (Muraven and

Baumeister 2000). Circumstances are not however always optimal, and when recovery during the day is lacking it will increase the risk for sleep disturbances (Tucker, Dahlgren et al. 2008). In turn, impaired sleep can lead to negative mood and feelings of frustration which may hamper recovery (Sonnentag, Binnewies et al. 2008).

### **2.1.5 Measuring stress**

There are many challenges to measuring stress, given that stress is both a physiological state and a subjective experience, perceived and experienced individually and affecting people differently. Hence it can be measured by either, or both, objective and subjective methods. It is however important to point out that even though physiological measures can be used to assess stress reactions, there is no biological definition of stress. Another aspect to keep in mind is that hormonal and physical effects differ depending on whether the stress is acute or chronic (Dhabhar and McEwen 1997). Measuring the subjective experience of stress is commonly done by different questionnaires and scales. One of the most widely used scales is the Perceived Stress Scale, a self-report measure assessing “the degree to which situations in one’s life are appraised as stressful” (Cohen, Kamarck et al. 1983).

The Maslach Burnout Inventory (Maslach, Jackson et al. 1996), pertaining to occupational burnout, and the Shirom-Melamed burnout Questionnaire (SMBQ) (Shirom 1989) are measures commonly used for assessing exhaustion and burnout. The latter is used in some of the studies included in this thesis and is described further in the methods section. The Maslach Burnout Inventory scale is a multidimensional construct consisting of 22 items to assess an individual’s experience of burnout. It measures 3 dimensions of burnout, emotional exhaustion, depersonalization and personal accomplishment. It was designed to assess burnout as a continuum, ranging from low to high scores and for this reason the initially determined cut-offs were removed in later editions as they were found to have no diagnostic validity.

There are also measures directed towards job stress specifically, such as the Job Content Questionnaire (Karasek, Brisson et al. 1998) which measures exposure to job related psychosocial risk factors, and the Effort Reward Imbalance Questionnaire (Siegrist 1996) measuring both physical, psychological and individual risk factors.

Long questionnaires can be difficult to get participants to answer and single question assessment is often utilized in order to minimize the burden on respondents (Elo, Leppänen et al. 2003). From a psychometric perspective a longer scale may be preferable, but many single-item measures have been found reliable (Fisher, Matthews et al. 2015). Another type of subjective measurement also employed in the present studies is the repeated rating of subjective experience of arousal (i.e. stress), for example every second or third hour over the day in a diary like questionnaire.

Objectively, stress can be measured through different biological markers of the stress response (Figuroa-Fankhanel 2014), of which cortisol is the most frequently used (King and Hegadoren 2002). Cortisol is a hormone involved in energy mobilization but it is also

instrumental in immune activity regulation (Chrousos and Gold 1992). All major organs and tissues have cortisol receptors and it can be measured in both saliva, urine and blood (Folkow 1997). Other measurable physiological markers of stress include heart rate variability, blood pressure, catecholamines, the inflammatory marker interleukin-6 and glucocorticoid receptor sensitivity (Dhama, Latheef et al. 2019). However, using biomarkers as a stress measure can be costly, in some cases invasive, and often requires trained health care professionals and/or specialized equipment. Another important limitation is the fact that changes may occur in the measured biomarkers for reasons not related to stress (Leka, Jain et al. 2010).

A different type of objective measure of stress is utilizing company records of sickness absence and various indicators of performance (e.g. work hours, task load etc.).

### **2.1.6 Gender and age differences in stress**

In the beginning of this section I mentioned some estimates of the prevalence of stress with the remark that stress is a very difficult experience to compare due to its subjective nature. Although perception of stress is very much determined by individual differences in vulnerability, appraisal and other factors, some patterns have been established on group level. When it comes to gender, women consistently report greater stress than men, both in terms of more frequent daily stressors (Almeida and Kessler 1998) and higher perceived level of stress (Klein, Brähler et al. 2016) (Cohen and Janicki-Deverts 2012). There are many possible explanations for these findings, including social, biological and psychological hypotheses (Mayor 2015) (Dalgard, Dowrick et al. 2006) (Lavoie JA 2012). Despite the fact that employment rates and average working hours among women have increased for the past 30 years, particularly among those with small children (SCB 2018), traditional gender- and family roles along with expected societal demands may obligate women to accept a larger part of childcare and housework responsibilities. This results in many women having a higher physiological workload and the possible work-family conflict might also increase levels of stress psychologically. Several studies suggest that the female gender is more sensitive to, and exposed to, more interpersonal stressors, especially stressors focused on health, family and peers (Hogan, Carlson et al. 2002) (Almeida, Wethington et al. 2002), whereas the male gender is associated with a higher exposure and sensitivity to more non-interpersonal stressors such as work- and school stress (Bakker, Ormel et al. 2011). However, Nazroo et al. (1997) showed that if the amount of commitment and involvement in home and family by men increased, these gender differences decreased (Nazroo, Edwards et al. 1997). Further, women are more likely to respond to stress with somatic and internalizing symptoms while men more often show externalizing symptoms (Aneshensel, Rutter et al. 1991) (Conger, Lorenz et al. 1993). Hence, the physical impact of stress is greater on women (American Psychological Association 2010). There is also evidence of a gender difference in the experience and perception of stress with women reacting more emotionally or strongly to certain stressors than men do (Purvanova and Muros 2010) and are also more likely to be exposed to and take on stressors of significant others (American Psychological Association 2010).



Being of younger age has also been associated with experiencing more stress (Cohen and Janicki-Deverts 2012) (AXA 2018). Despite the fact that stressors related to health is a common source of stress for older people (AXA 2017) (Osmanovic-Thunström, Mossello et al. 2015) and that long-term health conditions and having to deal with the loss of family and friends are naturally more prevalent with advancing age, older people generally report less stress (Akerstedt, Discacciati et al. 2019). For instance, a British national survey found that around 30% of people over 55 years of age reported not experiencing high levels of stress at all (AXA 2018). However, this may be explained more by a decrease in factors causing stress than by age per se, for instance, many aspects of work are commonly associated with stress and after retirement those types of stressors disappear.

## **2.2 SLEEP**

According to the allostasis stress theory (McEwen 1998), a stress response requires being followed by recovery in order to avoid the situation escalating towards allostasis. Sleep can be seen as the ultimate form of recovery and as previously discussed, therefore plays an essential part in determining the outcome of stress on health. Sleep is a complex physiological process, a state of disconnect from the environment characterized by physical inactivity, closed eyes and an increased threshold for arousal. It has been argued that during sleep the brain goes offline, meaning its different parts stops communicating with each other and the sensory input is decreased (Carskadon and Dement 2017). But the old notion that sleep is just rest for the body and brain has long since been abandoned. There are actually periods during sleep of very high brain activity, possibly even more so than when awake. We spend about one-third of our lifetime sleeping, so it is no wonder that the question of why we sleep have kept scientists busy for over a century. However, it wasn't until the early/mid twentieth century, with the discoveries of the circadian rhythm and rapid eye movement (REM) sleep for example, that sleep began its development into the broad research field it is today (Pelayo and Dement 2017). As sleep started to keep researchers awake at night performing all kinds of sleep studies (including some which might not be considered ethical today) (Patrick and Gilbert 1896) (Kollar, Pasnau et al. 1969) (Bliss, Clark et al. 1959), our knowledge of sleep and its functions grew substantially. Despite all these years of research we still don't have one definite answer to the question of why we sleep, but we do know that a lot of important things are happening while we sleep and a lot of unfavorable things happen when we don't. From an evolutionary perspective, it could be argued that since the time we spend sleeping prevents us from actively engaging in the basic activities necessary for our species to survive; eating, drinking (water) and passing on our genes, it clearly must be extremely important or all that time could have been used for above mentioned activities.

### **2.2.1 Theories of why we sleep**

Despite the lack of agreement among researchers there is however no shortage of theories as to what sleep's main function is. The theory of restorative function emphasizes changes in metabolism and growth, for example increased release of growth hormone and increased cell repair, while other theories suggest that conservation of energy by lowering thermoregulation

and metabolism is sleep's main function. While awake, many physiological functions are kept constant at optimal levels for the body's functioning. However, when we sleep, the physiological demands are reduced and many activities are reduced to conserve energy. For example, kidney function and urine production slow down and body temperature and blood pressure drop (Kryger, Roth et al. 2017). In physiological functions like breathing and cardiovascular activity, there is a pronounced variation during wakefulness (and during REM sleep), but during non-rapid eye movement (NREM) sleep they become very regular, giving the heart a chance to rest. Metabolite clearance, removing of waste products that accumulate in the brain during wake, has also been proposed as being a crucial function of sleep (Xie, Kang et al. 2013) and enhancing of the immune system through increased inflammatory response (Opp and Toth 2003) (Bryant, Trinder et al. 2004). Another possible immune enhancing process is increased skin blood flow, thought to improve skin's function as a barrier for pathogens (Van Someren 2006).

Sleep is also believed to be involved in memory consolidation (Grosmark and Buzsaki 2016) (Kaida, Niki et al. 2015) and functional magnetic resonance imaging (fMRI) studies have shown improved learning and cognitive performance on visuomotor task after sleep (Dang-Vu, Schabus et al. 2010) (Peigneux, Laureys et al. 2003). According to the synaptic homeostasis theory (Tononi and Cirelli 2003), the plastic processes that occur during wake result in a strengthening of synapses in many cortical circuits, and as a consequence the neurons' oscillations during sleep become strongly synchronized which is seen as large slow waves in the electroencephalogram (EEG). These slow waves are thought to downscale and renormalize synaptic strength to make way for changes, prevent excessive metabolic costs and preserve the relative strength between synapses to a level of optimal performance (Tononi and Cirelli 2006). There are also theories that focus less on the physiological changes and instead propose that sleep represents an adaptation to our ecosystem (Siegel 2009). As a species we are simply not at our best during the night and shouldn't be running around outside in the dark hunting, gathering, trying to find a mating partner or any activity requiring vision, as we would be more likely to become a predator's night snack or falling down a cliff for example.

### **2.2.2 Sleepiness and fatigue**

Loss of sleep, from total sleep deprivation to fragmented sleep, results in sleepiness (Gillberg 1995). Sleepiness can be defined as a physiological drive towards falling asleep, increasing with time awake and can be reversed or decreased with the quality and duration of sleep (Van Dongen, Maislin et al. 2003) (Akerstedt and Gillberg 1986). Sleepiness is not only determined by amount of sleep, it also follows our circadian rhythm with a pattern of lower levels during the day, except for a peak post-lunch, and higher in the evening. Immediately after waking up levels are often high regardless of the quality of sleep (Zulley and Campbell 1985). Although fatigue and sleepiness are two interrelated concepts, often used interchangeably in both research and daily language (Shahid, Shen et al. 2010), they can and should be distinguished from one another (Hossain, Ahmad et al. 2005) (Karshikoff, Sundelin

et al. 2017). Important differences between fatigue and sleepiness is that fatigue is a more diffuse state that cannot be reversed by sleep (Shahid, Shen et al. 2010) and can only be measured subjectively (Shen, Barbera et al. 2006) as an objective definition does not exist. Both states are however related to impairment in cognitive performance and both somatic and psychiatric disorders (Van Dongen, Maislin et al. 2003) (Belenky, Wesensten et al. 2003) (Bonnet and Arand 2003) (Kant, Bültmann et al. 2003) (Hossain, Ahmad et al. 2005).

### **2.2.3 Overview of normal sleep**

Sleep consists of two very different main states; non-rapid eye movement sleep (NREM) and rapid eye movement sleep (REM), which in the normal adult occurs in a series of cycles following a distinct pattern regulated by the ultradian process (Kryger, Roth et al. 2017). Every cycle lasts about 90-120 minutes and on average we go through 4-6 cycles per night (Patel, Sidhu et al. 2020). Assuming there is no sleep disorders present, sleep typically begins with NREM sleep. The NREM sleep occupies approximately 80 % of the total sleep time and is further broken down into three stages: N1, N2 and N3, depending on the characteristics of the brainwaves as measured with EEG. When awake, the EEG is characterized by a fast frequency (beta, >12 Hz), dominated by alpha rhythm (8-12 Hz) when the eyes are closed. As sleep progresses from wake state to the first stage of sleep, the activity pattern of most cortical neurons become much more synchronized and the firing rate decreases. During NREM the firing rate of the neurons alternate between high and low, resulting in large-amplitude oscillations called slow waves. These are especially prevalent during N3 sleep, which is therefore also called slow wave sleep. The first part of sleep contains more slow wave sleep while REM episodes generally become longer throughout the sleep. This is thought to be a way for the brain to prioritize deep NREM sleep in case the duration of sleep is insufficient.

The first stage of sleep, N1, has the lowest threshold for awakening and is characterized by theta activity (4 to 8 Hz), a low-amplitude, mixed-frequency activity on the EEG. After a few minutes N2 sleep appears, recognizable on the EEG by the presence of K-complexes and sleep spindles. N2 generally lasts about 25 minutes and composes almost 50 % of the total sleep time. K complexes are single, long, V-shaped waves that represents a transition into deeper sleep (Patel, Sidhu et al. 2020) (Nayak and Anilkumar 2020). Sleep spindles are rapid, separated discharges of 0.5 to 3 second neural activity generated in the thalamocortical loop, ranging from 11-16 Hz. They can occur in other stages of NREM sleep as well and their exact functions are not yet known but are thought to involve suppressed sensory signals at the thalamic level. There is also evidence of increased spindle activity after learning new things (Gais, Mölle et al. 2002) which has been suggested to strengthen the synaptic interconnections between neurons. Spindles also play a role in memory consolidation (Payne, Ellenbogen et al. 2008). As N2 sleep progresses into N3, or “slow wave sleep” (SWS), there is a gradual appearance of characteristic high amplitude (>75 microvolt) slow waves (delta waves, 0.5 - 4 Hz). This stage generally lasts 20 to 40 minutes and is commonly referred to as “deep sleep” as it has the highest awakening threshold. Slow wave sleep is considered very

important for recovery, this is when rebuilding and repairing of tissues, muscles and bone take place and the immune system is strengthened. Preceding the initial REM period that follows there is typically a short bout of N2 sleep. During REM sleep neuronal firing rate increases and the brain is actually highly active as opposed to the NREM sleep stages. EEG activity of REM sleep is very similar to wake stage with low-amplitude, high-frequency sawtooth waves and alpha rhythm. but as the name indicates, also contain the characteristic rapid movements of the eyes. Another important characteristic is that the skeletal muscles are temporarily paralyzed, with the exception of the eyes and diaphragmatic muscles used for breathing. However, whole-body oxygen consumption is increased during REM sleep (Parmeggiani 2007). Breathing frequency becomes faster and more irregular, heart rate and blood pressure increases and temperature regulation is shut off. REM sleep is associated with vivid dreaming and the paralysis is thought to prevent us from acting out our dreams. The initial REM period lasts for about 10 minutes, but for each cycle it gets longer and the last REM period can last as much an hour. The function of REM sleep is not yet fully understood but it likely involves memory consolidation (Boyce, Glasgow et al. 2016).

#### **2.2.4 Regulation of sleep and wakefulness**

Sleep is regulated mainly by two processes; the homeostatic drive for sleep and the circadian rhythm, also referred to as process S and process C (Borbély 1982). The homeostatic drive addresses the sleep need that accumulates during wakefulness. Prior amount of wake time and sleep efficiency affect SWS in the following sleep (Akerstedt and Gillberg 1986), meaning that having had a very fragmented, short sleep the night before or having stayed awake for a longer time will be compensated by deeper and longer sleep the next night and conversely, too much sleep, will give the opposite effect (Mezick, Matthews et al. 2009). Sleep pressure is proposedly related to the buildup of the neuromodulator adenosine (Holst and Landolt 2015), much to the joy of coffee producers worldwide since caffeine is an adenosine receptor antagonist and thus quite successfully inhibits sleep (Fredholm, Bättig et al. 1999).

The circadian rhythm on the other hand is a self-sustained oscillation driven mainly by the suprachiasmatic nuclei – SCN (Wright, McHill et al. 2013). It is also influenced by light/darkness and is unaffected by awake time (Morris, Aeschbach et al. 2012), and seems to be closely linked to metabolic, endocrine and other physiological processes like core body temperature. It works to ensure we are awake and sleeping at appropriate times based on the cycle of light and darkness. Light signals are transmitted to the SCN by the retinal ganglion cells and the SCN then projects to the pineal gland where the sleep promoting hormone melatonin is released (Hattar, Liao et al. 2002) (Reppert, Weaver et al. 1988). The rhythm of melatonin secretion is inhibited by light (Lewy, Wehr et al. 1980), the peak occurs between 2:00 and 4:00 am and gradually declines towards the morning. Blind people often show a desynchronized sleep-wake pattern due to absence of light cues (Hartley, Dauvilliers et al. 2018).

According to the flip-flop switch model of sleep-wake regulation proposed by Saper and colleagues (Saper, Chou et al. 2001), mutually antagonistic sleep-promoting and wake-promoting neurons, (e.g. orexin, also called hypocretin) form a switch circuit resulting in a rapid transition between behavioral states, producing the typical pattern of consolidated waking during the day and sleep at night. During wakefulness, the thalamus and cerebral cortex are activated by a network of cell groups. When it's time for the brain to sleep, this arousal system is shut off by a switch in the hypothalamus while other hypothalamic neurons act as stabilizers to this switch. Dysfunction in this circuitry or absence of stabilizers may result in sleep disorders like insomnia, narcolepsy and REM sleep behavior disorder.

Additionally, the immune system is involved in sleep regulation through cytokines such as interleukin 1 or tumor necrosis factor-alpha (Jewett and Krueger 2012). Research has suggested that sleep quality could be related to increased neuroinflammatory activity, as sleep provides a protective mechanism against the oxidative stress caused by wakefulness and sleep loss may result in a pro-inflammatory state (Irwin 2015) (Irwin, Carrillo et al. 2010) (Villafuerte, Miguel-Puga et al. 2015). There are however many factors that influence and interfere with our sleep patterns, for example age, alcohol and certain types of medicines. Other factors that can disrupt the natural sleep-wake cycle is exercise prior to sleep, artificial light exposure and perhaps most important, at least in the context of this thesis, stress.

### **2.2.5 Age and sleep**

With maturity in years comes an unavoidable change in sleep patterns and it is well established that age is a predictor of disturbed sleep (Ancoli-Israel and Roth 1999) (Leger, Guilleminault et al. 2000). Both subjective (Ohayon 2002) (Akerstedt, Fredlund et al. 2002) and objective indicators (Akerstedt, Schwarz et al. 2016) (Ohayon, Carskadon et al. 2004) of poor sleep increase. One aspect that may partly explain some of the age-related sleep changes is that age often comes with increased comorbidities (Ancoli-Israel 2005). Aging is associated with earlier circadian rhythm (Duffy, Zitting et al. 2015), decreased total sleep time (TST), wake after sleep onset (WASO), SWS, and lower sleep efficiency (SE) (Ohayon, Carskadon et al. 2004). Changes in sleep architecture have been found even in the individuals that do not consider themselves to be poor sleepers (Li, Vitiello et al. 2018) (Edwards, O'Driscoll et al. 2010). Interestingly, the age accompanying decrease in SWS seems to be notably more pronounced for men (Redline, Kirchner et al. 2004), even though women of all ages are found to have more sleep complaints than men. However, sleep restriction does not seem to have as negative an effect on older people as it does on younger, several studies have shown that daytime sleepiness and fatigue, which likely affects perceived restitution of sleep, decreases with age (Akerstedt, Fredlund et al. 2002) (Dijk, Groeger et al. 2010) (Akerstedt, Discacciati et al. 2018). They are also less affected by sleep loss when it comes to cognitive functions, such as reaction time and memory (Scullin and Bliwise 2015).

### 2.2.6 Measuring sleep

There is a variety of ways in which sleep and sleep-related impairments can be evaluated. Functional imaging studies provide a detailed examination of blood flow, regional metabolic rate and patterns of brain activation (Nofzinger 2005) (Dang-Vu, Desseilles et al. 2007). However, this method is very expensive and less accessible. The current gold standard for measuring sleep is by recording electrical brainwave activity through polysomnography (PSG) Using electrodes, the scalp's electrical activity (representing brainwaves) is recorded together with eye movement by electrooculogram (EOG) and muscle activity by electromyogram (EMG), and these signals are then analyzed in 30 second epochs that are each assigned a specific sleep stage. A common way of illustrating sleep architecture is through a graph, called a hypnogram, depicting the time spent in each sleep stage. Depending on the purpose of the sleep examination, other signals such as electrocardiogram (ECG), pulse (oximeter), respiratory rate and snoring detection can be added to give more information. The characteristics of the brainwaves and the presence or absence of eye movement and muscle tone define the different stages of sleep. Actigraphy is a non-invasive method of measuring sleep, usually in the form of a small wrist-worn unit. The sensor calculates sleep patterns by continuously measuring gross motor activity. It has the advantage of being relatively easy to administer and more practical for long term and ambulatory studies (Sadeh 2011). It may not provide as much information but has been shown to compare quite well to PSG (Marino, Li et al. 2013), although some studies indicate less accuracy in chronic conditions and insomnia (Taibi, Landis et al. 2013, Conley, Knies et al. 2019).

However, the most practical and widely used way to assess sleep-wake function is by asking people how they perceived their sleep, i.e. with self-report measures, such as the well-established and validated The Karolinska Sleep Questionnaire (KSQ) (Nordin, Åkerstedt et al. 2013), which is described further in the methods section of the thesis. There are different types of self-rated instruments, some assess temporal and quantitative aspects of sleep on habitual or daily basis like sleep-wake diaries (see method section for description) while others are focused on specific sleep disorders like sleep apnea (Maislin, Pack et al. 1995) (Netzer, Stoohs et al. 1999), narcolepsy (Douglass, Bornstein et al. 1994) or insomnia. With approximately 30-40% of adults complaining of insomnia (Ohayon 2002), there is a multitude of scales and questionnaires addressing said sleep disorder, for reviews of different measures see for example Buysse et al. 2006 and Moul et al. 2004. Some of the most widely used instruments for assessing and screening for insomnia symptoms in both clinical and research settings are the Insomnia Severity Index (Bastien, Vallieres et al. 2001) and the Pittsburgh Sleep Quality Index (Buysse, Reynolds III et al. 1989). The Pittsburgh Sleep Quality Index measures self-reported sleep quality and sleep disturbances. It consists of nineteen individual items, creating seven subscale scores (sleep quality, duration, latency, efficiency, sleep disturbances, sleep medication use, and daytime dysfunction), together generating one overall sleep quality score ranging from 1-21, where a score >5 denote a potential sleep problem. The Insomnia Severity Index is an instrument comprised of seven items designed to assess the perceived severity of insomnia symptoms of both night- and

daytime as well as the degree of distress the sleep problem causes. Subjective measurements have the advantage of being cheap, non-invasive, not requiring much more equipment than a printer and allows for a larger study sample. Compared to PSG it stands up fairly well (Zinkhan, Berger et al. 2014), but there is always a greater risk for response bias when using subjective measurements as well as other methodologic challenges. Also, the reduced awareness during sleep, and the brief retrograde amnesia associated with the sleep onset transition (Wyatt, Bootzin et al. 1997) effectively limits the ability to correctly recall and report quantitative variables like for example number of awakenings and sleep latency. Other challenges include the considerable day-to-day variation in sleep-wake function and the fact that sleep quality can be characterized in multiple ways, from duration and efficiency to perceived quality and daytime impairment.

Another approach to measuring sleep is by assessing the consequences of sleep disturbances. Sleepiness is considered a reliable marker for measuring insufficient sleep (Akerstedt, Anund et al. 2014). Sleepiness can be physiologically measured by polysomnography as latency to stage 1 sleep with the Multiple Sleep Latency Test (MSLT) (Carskadon and Dement 1982) or the Maintenance of Wakefulness Test (Mitler, Gujavarty et al. 1982). It can also be measured subjectively by self-reports. The most widely used self-report instrument for measuring sleepiness is the Epworth Sleepiness Scale (Johns 1991) (Johns 1992), which is a scale rating the tendency to fall asleep in different situations. It is considered easy to use and score, but has also been criticized for showing limited correlation with objective measures of sleepiness, e.g. the Multiple Sleep Latency Test (Chervin, Aldrich et al. 1997) (Olson, Cole et al. 1998), and for the content not being entirely relevant (excluding some common situations where sleepiness may occur while including some less frequently encountered) (Miletin and Hanly 2003). Examples of other commonly used subjective measures are the Stanford Sleepiness Scale (Hoddes, Zarcone et al. 1973) or the Karolinska Sleepiness Scale (KSS) (Akerstedt and Gillberg 1990). The KSS is used in the studies in this thesis and described in more detail in the methods section.

### **2.2.7 Sleep quality and sleep health**

The concept sleep quality is difficult to measure objectively as it encompasses both qualitative and quantitative aspects and there is no real consensus regarding what a good sleep quality is exactly. Harvey et al. (2008) proposes that assessing sleep quality may require including variables regarding waking and daytime functioning following sleep as well. In a cross-sectional study examining the meaning of sleep quality they found that the absence of sleepiness and feeling rested and restored, not only upon rising but also throughout the day was emphasized by both insomniacs and normal sleepers. Fewer (perceived) awakenings during the night were also identified as a determinant of good sleep (Harvey, Stinson et al. 2008). Subjective ratings of poor sleep are usually associated with objective measures of sleep discontinuity (lower sleep efficiency, more awakenings and WASO) (Baglioni, Regen et al. 2014) (Akerstedt, Schwarz et al. 2016) (Saletu 1975). Objectively, both continuity of sleep and duration of sleep are important aspects of sleep quality (Akerstedt, Hume et al.

1994) (Akerstedt, Nilsson et al. 2009). Long sleep has also been related to a higher subjective sleep quality (Akerstedt, Schwarz et al. 2019). Those habitually sleeping too long or too short are both however more commonly experiencing insomnia symptoms and a significantly increased mortality risk compared to those who stick to the recommended amount of sleep (7–8 h) (Grandner and Kripke 2004) (Hirshkowitz, Whiton et al. 2015). That number is in line with research from Kripke et al (Kripke, Garfinkel et al. 2002) who found that the lowest mortality was among those sleeping 7 hours per night.

A newer and related concept is ‘sleep health’. Buysse (Buysse 2014) argues that good sleep is more than just the absence of sleep disorders and emphasizes the positive role of sleep in overall health. He proposes that sleep health can be defined as: “a multidimensional pattern of sleep-wakefulness, adapted to individual, social, and environmental demands, that promotes physical and mental well-being. Good sleep health is characterized by subjective satisfaction, appropriate timing, adequate duration, high efficiency, and sustained alertness during waking hours”. This definition is based on the dimensions of sleep that are most clearly associated with physical, psychological as well as neurobehavioral well-being, and has the advantage of being measurable.

### **2.2.8 Disturbed sleep**

Insufficient sleep is becoming increasingly common in modern societies, for instance due to the rise of smart phones and tablets (Do, Shin et al. 2013), artificial lightning and excessive or displaced work hours (Akerstedt, Kecklund et al. 2007) (Ingre, Kecklund et al. 2008) (Kronholm, Partonen et al. 2008). In Sweden, sleep problems are common, with studies showing approximately 25-30 % of Swedish adults reporting having frequent insomnia symptoms (Mallon, Broman et al. 2014) (Ohayon and Bader 2010). These estimates are in line with other population-based surveys (Leger and Bayon 2010) (Morin, LeBlanc et al. 2006) (Ohayon and Partinen 2002). With such a big part of the adult population reporting frequent complaints of poor sleep, some researchers even call it a global epidemic (Bin, Marshall et al. 2012) (Walker 2019). Sleep problems also seem to be more common now than over the past 40 years (Kronholm, Partonen et al. 2008) (Rowshan Ravan, Bengtsson et al. 2010). Two population-based studies in Sweden (Broman, Lundh et al. 1996) and Finland (Hublin, Kaprio et al. 2001) reported that insufficient sleep was a fairly frequent sleep problem, affecting 12% and 20% of the population respectively. Several studies show that people sleep less now than a few decades ago (NCHS 2005) (Ford, Cunningham et al. 2015) (Kronholm, Partonen et al. 2008). However, trends of global average habitual sleep duration over time shows a mixed pattern (Bin, Marshall et al. 2012). For example, in Sweden the prevalence of long sleep has increased, while Italy, USA and Canada have had a decrease (Rowshan Ravan, Bengtsson et al. 2010) (Bin, Marshall et al. 2013). In a US national Health survey, results showed that not only had habitual long sleep decreased, at the same time the prevalence of short sleep durations had drastically increased (Jean-Louis, Williams et al. 2014). There are also studies that have found no change in sleep patterns over the years (Bonke 2015) and other that claims it is only the quality of sleep that has gone down, while



average sleep duration has remained constant (Hoyos, Glozier et al. 2015) (Youngstedt, Goff et al. 2016). The most obvious sign of sleep loss is of course feeling tired, most likely looking tired (Sundelin, Lekander et al. 2017), and maybe even looking less attractive and trustworthy (Holding and Sundelin 2019). According to a review by Ohayon (2008) excessive sleepiness was prevalent among about 5% to 15% of the adult population. Sleepiness can have more serious and costly consequences than negatively affecting your social life (Sundelin, Lekander et al. 2017) though, in that it contributes to traffic and work-related accidents (Akerstedt, Philip et al. 2011) (Philip and Akerstedt 2006). Disturbed sleep is also strongly linked to a high utilization of health resources (Daley, Morin et al. 2009) and sickness absence (Lallukka, Haaramo et al. 2013) as well as to diabetes II, cardiovascular disease, and mortality (Buysse, Grunstein et al. 2010). Sleep disorders like insomnia can cause increased sympathetic nervous activity and vascular endothelial dysfunction which is the probable reason behind the increased risk for cardiovascular disease (Khan and Aouad 2017). The increased SNS activity leads to increased noradrenaline and adrenaline production, and in extension also result in decreased critical immune cells (Irwin 2019) and a rise in inflammatory biomarkers (Haack, Sanchez et al. 2007). Not getting enough sleep may also impair glucose metabolism (Schmid, Hallschmid et al. 2015) and can influence hormone levels, including increased cortisol and decreases in testosterone, thyroid stimulating hormone, and growth hormone (Briançon-Marjollet, Weiszenstein et al. 2015) (Mullington, Haack et al. 2009). Cognitive functions like perception, attention and creativity are also negatively affected (Wickens, Hutchins et al. 2015) (Jackson and Van Dongen 2011) (Killgore 2010) as well as our mood and emotional reactions (Beattie, Kyle et al. 2015) (Deliens, Gilson et al. 2014). Furthermore, learning and the ability to consolidate memories decreases when sleep deprived (Yoo, Hu et al. 2007).

## **2.3 SLEEP AND STRESS**

Stress is a reaction to a threat to homeostasis and sleep is a key function in maintaining homeostasis. Acute sleep deprivation on the other hand is clearly a threat to this balance and a trigger to a response from the stress-system. With the physiological activation produced by the stress response it seems logical to expect a connection between disturbed sleep and stress. There are numerous prospective (de Lange, Kompier et al. 2009) (Akerstedt, Nordin et al. 2012) (Magnusson Hanson, Theorell et al. 2009) and cross-sectional questionnaire studies linking stress to sleep complaints (Kalimo, Tenkanen et al. 2000) (Doi, Minowa et al. 2003) (Akerstedt, Knutsson et al. 2002) (Morphy, Dunn et al. 2007) (Hall, Buysse et al. 2000). All indicate a clear negative correlation between stress and sleep quality. However, in most research on stress and sleep the stressor has been of experimental nature (Kim and Dimsdale 2007) and except for some cross-sectional epidemiological studies, have not involved naturally occurring daily stress (Knudsen, Ducharme et al. 2007) (Ancoli-Israel and Roth 1999) (Ribet and Derriennic 1999) (Urponen, Vuori et al. 1988) (Akerstedt, Fredlund et al. 2002).

Insomnia is one of the most common sleep disorders and exposure to both acute and long-term stress is one of the most common causes (APA 2013) (Morin 2003). According to the International classification of sleep disorders (AASM 2014), acute stress can cause “adjustment insomnia”, and the consequences of chronic exposure can lead to “primary insomnia”. Also, hyperarousal is included as a cause in contemporary models of sleep disturbances (Riemann, Spiegelhalder et al. 2010). Stress is thus an established cause of sleep problems (Halonen, Lallukka et al. 2017) but we don’t know whether people attribute their disturbed sleep to stress to a larger extent than to other factors potentially disrupting sleep. Work is often reported as one of the most common stressors (AXA 2018) (Danielsson, Heimerson et al. 2012) (UNISON 2017) but PSG studies of the relationship between work stress and sleep are rare. Linton & Bryngelsson (2000) found self-reported work stress to be the most frequent cause of sleeping problems (Linton and Bryngelsson 2000) and high work demands and negative psychosocial work conditions have been related to lower sleep quality and insomnia (de Lange, Kompier et al. 2009) (Linton 2004) (Jansson and Linton 2006). Periods of high work stress have also been shown to increase sleepiness (Dahlgren, Kecklund et al. 2005). Further, according to the Swedish Work Environment Authority one in five Swedish workers report negative effects on their sleep due to work factors (including both physical and psychosocial factors) (Arbetsmiljöverket 2012) and a nationally representative sample found a positive association between job stress and frequency of poor sleep quality (Knudsen, Ducharme et al. 2007). Other causes may be small children (Skinner and Dorrian 2015), work hours (Salo, Ala-Mursula et al. 2014), leisure activities and social life (Basner, Fomberstein et al. 2007), poor health (Barros, Lima et al. 2019), use of technology and media (Thomee, Harenstam et al. 2012), among others. For example, smartphone and similar activities can cause disturbed sleep in several ways, for example through trading sleep time to keep up with work or peers on social media or by causing cognitive arousal and via light exposure from the screen. Feeling pressure to always be available online, answer emails and take phone calls outside of work is a commonly reported stressor and also likely a mediator in the relationship between using technology and sleep disturbances (Thomee, Harenstam et al. 2011). This type of accessibility stress has been found to be higher among young people and men (SCB 2018).

### **2.3.1 Effects of stress on specific aspects of sleep**

Questionnaire studies of stress and sleep show a clear connection, however, in terms of polysomnography, there are not as many available studies, particularly involving real-life stress. Studies using experimental stressors such as impending exams have found shorter sleep duration (Holdstock and Verschoor 1974), reduced SWS (Lester, Burch et al. 1967) and increased REM (Becker-Carus and Heyden 1979). Exposure to long-term stress have been related to reduced slow wave sleep, increased stage 1 sleep and more awakenings (Ekstedt, Soderstrom et al. 2009), and the number of microarousals have been related to higher levels of sleepiness in burnout patients (Ekstedt, Åkerstedt et al. 2004). Stress has also been connected to reduced objective and subjective sleep duration in many studies (Hrozanova, Moen et al. 2019) (Johnson, Lisabeth et al. 2016) (Chin, Guo et al. 2015).

If we are interested in naturally occurring stress, a design where sleep is recorded in a home setting is probably more relevant with respect to stress responses than recording sleep in a laboratory. In a PSG study using such a design to compare nights after high and low ratings of work stress it was found that stress and rumination at bedtime correlated with lower sleep efficiency and increased latency to deep sleep (Åkerstedt, Kecklund et al. 2007). Anticipation of stress seems to be an important factor in the relationship between stress and sleep.

Increased fragmentation of sleep and reduced SWS have been found during nights before surgery (Edéll-Gustafsson 2002), unpleasant early mornings (Kecklund and Åkerstedt 2004) (Kecklund, Åkerstedt et al. 1997) and nights with on-call duty (Torsvall and Åkerstedt 1988). Previous research demonstrates a relationship between sleep quality and repetitive self-focused thoughts on stressful events (e.g. perseverative cognitions/rumination) at bedtime (Thomsen, Yung Mehlsen et al. 2003) (Guastella and Moulds 2007) (Cropley, Dijk et al. 2006) and several studies indicate a mediating role of perseverative cognitions between stress and disturbed sleep (Berset, Elfering et al. 2011) (Van Laethem, Beckers et al. 2016).

There is still a lack of knowledge in many areas regarding the relationship between stress and sleep, especially in terms of PSG studies concerning work stress and sleep, how age and gender relates to stress disturbed sleep and the role of individual vulnerability. There is a need for more studies exploring the causes of disturbed sleep, and of what individuals themselves attribute sleep disturbances to. We know through previous research that sleep problems increase with age (Groeger, Zijlstra et al. 2004) (Mallon, Broman et al. 2014) and that women report more sleep complaints (Leger, Guilleminault et al. 2000) (Åkerstedt, Fredlund et al. 2002) and more stress (Klein, Brähler et al. 2016) than men do, but we have no information regarding possible age- or gender differences in which causes we attribute sleep disturbances to, and on how stress-disturbed sleep is associated with age, or gender. Furthermore, the direction of the relationship between stress and sleep is not clear, whether stress leads to sleep problems or poor sleep results in more stress, though evidence suggests the relationship may be bi-directional. There are studies showing that impaired sleep predicts both increased vulnerability to stress and increased levels of stress (Schwarz, Gerhardsson et al. 2018) (Zaslavsky, LaCroix et al. 2015) (Åkerstedt, Garefelt et al. 2015) (Magnusson Hanson, Åkerstedt et al. 2011). This question should be approached through a study of day-to-day variations in stress and sleep across many days.

### **2.3.2 Individual vulnerability**

Another factor that much be taken into consideration when measuring stress is that not everybody reacts the same to identical stressors. Individual differences in vulnerability to stress have been related to both subjectively and objectively measured sleep disturbances (Drake, Richardson et al. 2004) and many studies have demonstrated a link between insomnia and sleep reactivity, e.g. stress-related sleep disturbance, suggesting that insomnia is related to a greater sensitivity to stress (Drake, Friedman et al. 2011) (Nakajima, Okajima et al. 2014) (D. Jarrin 2013). Not everybody exposed to stress experience stress-disturbed sleep, some people may be more susceptible to the effects of chronic stress (Drake, Richardson et

al. 2004). A longitudinal study (Vahtera, Kivimäki et al. 2007) showed that a tendency to react strongly to stress predicted later sleep disturbances, and Bonnet et al (2003) found increased sympathetic activity in those who responded to different stressful situations with poor sleep (Bonnet and Arand 2003). Unfortunately, some of us will have a harder time thanks to our genes, sleep reactivity to stress was found to be 43% and 29 % heritable among men and women respectively (Drake, Friedman et al. 2011). On the other hand, some individuals have the ability to adapt to negative triggers or events in a positive way through not only psychological skills but also through social support systems as a coping strategy (Friborg, Hjemdal et al. 2003).

### **2.3.3 Weekends/days off and recovery sleep**

The time available for sleep is many times limited by work schedules and different leisure activities, and it seems logical that we therefore sleep shorter on weekdays compared to days off (Basner, Fomberstein et al. 2007) (Knutson, Phelan et al. 2017) (Söderström, Ekstedt et al. 2004). One might also expect a reduction in stress during days off work. Consequently, for most people, the weekend is considered a window of recovery (Fritz and Sonnentag 2005). Some studies show that self-reported weekend sleep is approximately 1 hour longer than weekday sleep (Basner, Fomberstein et al. 2007) (Knutson, Phelan et al. 2017) while others have found an average difference between weekday and weekend sleep duration of 0.3 h (Groeger, Zijlstra et al. 2004) (NSF 2002). In the two latter surveys, about 20 % reported sleeping less than 6 h on weekdays. Corresponding figures for weekends were 17% and 14 % for the two surveys respectively. However, 22 % of the British respondents and a large proportion of the US population, 44%, reported excessive sleep on weekends (> 8 h) which could be a way to recover the accumulated sleep loss from the week. Studies show that chronic sleep loss can add up over time resulting in an impairment resembling that of total sleep deprivation (Belenky, Wesensten et al. 2003) (Cote, Milner et al. 2009) (Van Dongen, Maislin et al. 2003).

Most studies on sleep duration concerns weekdays and there is very little knowledge whether sleep before a day off, weekend sleep, is ‘better’ than sleep between workdays. There are also very few representative studies regarding sleep duration and a lack of knowledge regarding the effect of stress on sleep duration on weekends compared to weekdays. From the previous section it seems that we lack 1) a representative study of stress disturbed sleep and its links to age and gender, 2) a real life home recorded study of PSG recorded sleep before and during a period of work stress, 3) a PSG home recorded study before a day off and 4) a study of day-to-day covariation of stress and sleep across several weeks.

### 3 AIMS

The overall aim of the thesis was to examine the relationship of naturally occurring, day-to-day stress and sleep (objective and subjective), both in general and regarding the role of individual vulnerability to stress. An additional overall aim was to examine whether stress is seen as a major cause of disturbed sleep in the general population.

#### 3.1 SPECIFIC AIMS IN THE DIFFERENT STUDIES

Study I and II is part of a larger project investigating the influence of psychosocial stress on both objective and subjective sleep in teachers. It was hypothesized that high stress would result in impaired sleep and higher levels of sleepiness. Specific aims of study I:

- 1) Study the effect of different intensity of daily real-life work stress on objective sleep measures and perceived quality of sleep.
- 2) Study the diurnal pattern of reported sleepiness during periods of high and low stress, as well as indicators of mood and performance.
- 3) Investigate potentially moderating effects of individual differences in vulnerability to stress related sleep disturbances.

In study II the overall aim was to compare objectively recorded sleep during the workweek to a sleep after a workday but followed by a day off/weekend. The hypothesis was that Friday night sleep would be followed by lowered stress and sleepiness. Specific aims:

- 1) Examine whether objective measures of sleep and perception of sleep quality on sleep following a workday differed between nights followed by a workday and nights before a day off (Fridays).
- 2) Investigate if subjective ratings of stress and sleepiness was lower on days following Friday night sleep compared to weekdays.

Study III aimed to investigate how daily variations in self-reported stress related to daily variations in perceived sleep quality the next morning. It was hypothesized that day/evening stress would result in reports of poor sleep the following morning. Specific aims:

- 1) Study the relationship between subjective stress and self-reported sleep quality on a day-to day basis.
- 2) Add to the knowledge gap regarding causation and possible bidirectionality of the association between stress-sleep disturbance.

The aim in study IV was to examine the association between stress and disturbed sleep in a representative national sample with regard to age and gender. The hypothesis was that stress would be associated with more disturbed sleep and shorter weekday sleep duration, whereas the weekend sleep duration effect was not possible to predict. Specific aims:

- 1) Explore the prevalence of stress-disturbed sleep and the causes attributed to disturbed sleep in relation to age and gender.

- 2) Examine the association between stress, sleep disturbances and sleep duration (during both weekend and weekend).

## 4 MATERIAL AND METHODS

### 4.1 PARTICIPANTS

Study I and II are based on the same study sample of junior high school and high school teachers. Teachers constitute a group that reports high work-related stress (Arbetsmiljöverket 2010) and were assumed to be able to predict work periods of high and low stress. The stress involved the considerable increase in workload towards the end of the semester with examination and grading. All were recruited through advertisements at schools in the Stockholm area and through contacts. A total of 36 individuals were included in the first study, of whom 28 (7 men, 21 women, mean age 41 years (standard deviation: 9, range: 27–62)) completed the entire study. Nineteen were married/cohabitant, and three had small children living at home (>7 years old). All participants from study I were asked to participate in an additional study period and 17 participants chose to continue. The sample in study II thus included 17 participants (4 men and 13 women), mean age 48 years (standard deviation: 9, range: 32–67), 12 were married/cohabitant, and two had small children. All participants included in the study were working full time, reported good health, a non-sedentary lifestyle and had no sleep complaints or used any medication known to interfere with sleep. They were all non-smokers and reported a moderate alcohol intake. Participants with sleep disorders, ongoing depression or stress related disorders were excluded from the study. A habituation sleep was recorded before the study started, during which all participants were thoroughly screened for any sleep disorders using heart rate monitoring, SaO<sub>2</sub> (finger pulse oximetry), airflow (nasal cannula), respiratory effort bands, and anterior tibialis EMG (for detection of periodic limb movements). Eight participants were excluded from the study; one fulfilled criterion for depression and remaining seven were excluded after discovery of sleep disorders during the habituation night. Bedtime and time of rising was in accordance with their habitual pattern and they were asked to abstain completely from beverages containing caffeine after 15:00 on the day of the sleep recording and from alcohol from 2 days prior to the recording.

The participants in study III were recruited through advertisements and contacts. A total of 50 individuals between the ages of 18–61 years (mean age:  $43.5 \pm 16.4$ ) participated, there were slightly more women (59 %) than men. A majority, 68%, were married or cohabiting, 30% had a university education, 70% were employed and the remainder were students (22%), retired (6%), or unemployed (2%). Before inclusion all participants were screened for sleep disorders and insomnia symptoms, cardiovascular disease, psychiatric disease, diabetes or obesity, and 12 % were excluded due to depression and sleep disorders. There was no use of hypnotics, sedatives or any other sleep interfering medicine. Reported habitual sleep quality was 3.7, which is above the mean of the Swedish population (3.0) (Akerstedt, Ingre et al. 2008).

The study IV sample consisted of 1550 Swedish residents, proportionally stratified for age and gender and representative for the population. The response rate was 72.8%; a total of

1128 subjects between the age of 18-84 years (mean age  $47.8 \pm 18$  years) of which 52.1 % were women, completed the interview. Any participants that had insufficient fluency in Swedish, impairment of speech or hearing, or an illness that might affect their ability to participate in the interview were excluded. As a high resolution of age groups was prioritized for descriptive data of stress and stress disturbed sleep across ages, the sample was divided into 6 groups with cut-offs at 25, 35, 45, 55 and 65 years of age. All groups were not equal in sample size and therefor age was also split by the median (46 years of age) and analyzed as a dichotomized variable of a younger (18-46 years) and an older group (47-84 years). The younger group consisted of 560 persons (281 men, 279 women), and the older group of 568 persons (259 men, 309 women).

## **4.2 OBJECTIVE MEASURES**

### *Polysomnography*

Ambulatory polysomnographic recordings were carried out in the participant's home by a trained research assistant using portable Embla recorders (Flaga HF/Medcare). The electrodes used were Ag/AgCl, with two electroencephalogram (EEG) derivations C3-A2 and C4-A1, one bipolar chin electromyographic (EMG) derivation and two electro-oculogram (EOG) oblique derivations. The sampling rate was 100 Hz and for one channel a 0.8 Hz high pass filter was applied before sleep scoring for the purpose of reducing low frequency artifact impact. Sleep stages were scored visually in 30-second epochs and according to the American Academy of Sleep Medicine (AASM) manual (Iber, Ancoli-Israel et al. 2007). The standard parameters of PSG were computed: total sleep time (TST), minutes and percentage of sleep stages 1-3 and REM, wake after sleep onset (WASO), i.e. time awake during the sleep period between sleep onset and final awakening, Sleep efficiency (SE; TST/time in bed), awakenings, arousals and stage transitions (number per hour of TST), sleep latency (SL; time in minutes to onset of first sleep), SWS latency (minutes from sleep onset to first stage 3) and REM latency. Sleep spindles and arousals were scored according to the AASM criteria (Iber, Ancoli-Israel et al. 2007). For sleep spindles the criterion was a duration of 0.5 s with 11-16 Hz activity. Arousals were defined as an EEG shift from stage 2, 3 or REM to at least alpha activity preceded by a minimum of 10 seconds of uninterrupted sleep. For an arousal to be scored it had to last for more than 3 seconds, and less than 15 seconds, during REM sleep, an increase in EMG activity was also required. Sleep-onset latency was scored as minutes from 'eyes closed' to the first of at least three consecutive sleep epochs. All participants were screened for breathing pauses lasting 10 seconds or more with at least 3 % desaturations to rule out sleep apnea. All sleeps from different conditions in a study, i.e. high/low stress and weekday/weekend, were scored by the same person.



### *Actigraphy*

In study I and II the participants sleep pattern was followed the days around the polysomnographic sleep recording through an Actiwatch (Cambridge Neurotechnology, Cambridge, UK) worn on the non-dominant wrist. Study III also used actigraphy but because there was a lot of missing data it was never used in the analysis. The actigraph was only taken off during baths or showers. Participants were instructed to press a marker button on the actigraph when they went to sleep and when they woke up to help determine the sleep latency and differentiate between inactivity lying down and sleep and naps.

### *Cortisol*

In study I, cortisol was measured in saliva using Salivette, Sarstedt Ag & Co., Nümbrecht, Germany. Salivary cortisol has shown high correlations with plasma measures (King and Hegadoren 2002). Samples were obtained for each condition during the evening and morning of the PSG recordings. The first sample was collected at bedtime, followed by samples immediately after awakening, 15 minutes after awakening and 30 minutes thereafter. The participants administered the samples themselves, marked them with date and time according to the given instructions and stored them in a refrigerator until collected by the research assistants in the morning when collecting the PSG equipment. This was followed by one sample at noon and one at bedtime which were then sent by mail to the laboratory the next day. The samples were obtained by participants keeping a cotton swab in their mouths for 1 min and then placing it in a plastic tube. Participants were instructed to avoid food and drink for 30 min before taking the samples. Ten percent of the samples were lost due to the participants forgetting to give all samples. The cortisol samples were analyzed by radioimmunoassay using the Spectria coated tube radioimmunoassay (FI-02101 Orion Diagnostica, Espoo, Finland).

## **4.3 SUBJECTIVE MEASURES**

At the start of studies I-III every participant was administered a background questionnaire. Among the demographic variables were: age, gender and employment. It also included questions about current work conditions, sleep characteristics and habits, health and medical conditions, physical activity during leisure time, alcohol consumption, height, and weight. The questionnaire also contained several scales that are described below.

### *The Karolinska Sleep Questionnaire*

The Karolinska Sleep Questionnaire (KSQ) (Åkerstedt, Ingre et al. 2008) (Nordin, Åkerstedt et al. 2013) was used to assess the participants habitual sleep in studies I-III. The KSQ has been validated in insomnia groups and has a Chronbach alpha of 0.73 (Åkerstedt, Ingre et al. 2008) (Åkerstedt, Knutsson et al. 2002). It contains questions about habitual sleep patterns, overall quality of sleep, restless sleep, difficulties initiating and maintaining sleep (repeated awakenings), premature awakening and daytime sleepiness (difficulties staying awake/dozing off and sleepiness at work and/or leisure time). The participants reported their habitual

bedtimes, wake up times, how long time it normally takes them to fall asleep (sleep latency), their usual sleep duration for workdays and weekends and the preferred sleep length they needed to feel completely rested.

#### *The Ford Insomnia Response to Stress scale*

The FIRST scale (Ford Insomnia Response to Stress), developed by Drake et al. (2004), is an instrument for assessing individual sensitivity to stress related sleep disturbances. It is comprised of nine questions which measures the likelihood of experiencing sleep disturbances in response to commonly experienced stressful situations. Ratings are made on a four graded scale (1= not at all, 4= very affected). It was used in study I to identify subjects with high and low sensitivity to stress disturbed sleep. The cut-off point was set at 2.5 so that the group classified as having high sensitivity ( $>2.5$ ) would include only scores higher or equal to a moderate stress response in the scale. Thirty-two percent of the participants was classified as having high sensitivity (HS) and the rest, 68%, as having low sensitivity (LS). The two groups differed in terms of gender, with the high sensitivity group containing only women whereas the low sensitivity group was mixed ( $P < 0.036$ ).

#### *The Hospital Anxiety and Depression Scale*

The Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith 1983) was used in study III to obtain measures of depression and anxiety. In study I and II it was used for screening purposes only. Although HADS is targeted more towards the general population it correlates well with other scales targeting more clinical groups (Hopwood, Howell et al. 1991) (Lisspers, Nygren et al. 1997), and has high internal consistency (Chronbach alpha  $>0.81$ ). The scale consists of two dimensions, anxiety and depression, with seven questions each. The response alternatives are rated on a scale from 0-3 (higher values indicate more symptoms). The cut-off for exclusion from the study was the same as is used clinically as an indicator of depression or anxiety symptoms, a sum of 11 or more on each scale.

#### *The Shirom–Melamed Burnout Questionnaire*

The Shirom–Melamed Burnout Questionnaire (SMBQ) (Shirom 1989) (Melamed, Kushnir et al. 1992) was included in the background questionnaire in study I and II for screening purposes and was used in study III for assessing burnout and exhaustion. It measures the extent to which a person experiences different symptom of exhaustion for the majority of the day, to be rated on a seven-point scale from 1-7 (almost never to almost always). The scale contains 22 questions that comprises four subscales; “Physical Fatigue” (8 items), “Cognitive weariness” (6 items), “Tension” (4 items), and “Listlessness (2 items)”. The total score is averaged for a value of global burnout, or for each subscale. Higher scores indicate more severe symptoms of burnout and the cut-off value is 3.75.

### *The Karolinska Sleep Diary*

The participants completed the Karolinska Sleep Diary (KSD) for 3 days (study I) and 2 days (study II) in conjunction with the polysomnographic sleep recordings. In study III the diary was used daily for six weeks. The KSD have shown good correlations with objective sleep parameters when validated against PSG (Akerstedt et al., 1997). The diary consists of one part to be answered in the morning, assessing the previous sleep, and one part to be answered before bedtime with questions regarding behaviors and states during the day and at bedtime that might affect sleep. The daytime part contains items about sleepiness, stress and subjective arousal, alcohol and coffee consumption, work day or not, subjective health and fatigue (1–7; very poor–very good), anticipated sleep and anticipation for next day (1-5; very poor - very good sleep). The following 4 questions, “*Forgotten something one were meaning to do/say*”, “*Difficulty concentrating*”, “*A feeling that there is something one is supposed to remember*”, with answers rated from 1-3 (1= several times, 2= sometimes, 3= no) and “*Difficulty getting rid of thoughts of work in the evening* (1= very much – 4= not at all), formed a cognitive complaints index. Two types of stress ratings were used. One involved rating arousal/stress every two hours (study I and II) or three hours (study III) during the day on a scale from one (no stress at all/very relaxed) to nine (maximum stress/very wound-up) (Söderström, Ekstedt et al. 2004). The other item was “*stress/worries at bedtime*” (1-5; none - very much), thought to reflect rumination around stress and other problems at bedtime, which has been found to be an important factor in insomnia (Harvey, Tang et al. 2005). The latter has previously been used for selecting stressful and non-stressful nights for PSG recordings to compare sleeps of high and low stress periods (Akerstedt, Kecklund et al. 2007). The daytime variables used in the study were mainly the ratings of the day before the PSG night.

The sleep diary rated in the morning contains questions about wake- and bedtimes, subjective sleep quality, depth and duration of the sleep, number of awakenings and feelings at awakening. The sleep items (*sleep quality*, *calmness of sleep*, *ease of falling asleep*, and *sleep throughout the allotted time*) formed a sleep quality index (SQI) and questions regarding the awakening, “*ease of waking up*”, “*restless sleep*”, “*sufficient sleep time*”, formed an awakening index. Response alternatives ranged from 1- 5; very bad - very good. The SQI correlates well against objective sleep parameters (Akerstedt, Hume et al. 1997) and initial testing of the SQI showed a mean intraindividual correlation of  $r_{\text{mean}} > 0.60$  (Akerstedt, Hume et al. 1994) across 14 days. For study III, a measure of TST for each night was derived using the responses given on the questions about time of going to bed, time of awakening and the time it took to fall asleep.

### *The Karolinska Sleepiness Scale*

The Karolinska Sleepiness Scale (KSS) (Akerstedt and Gillberg 1990) measures the level of sleepiness on a scale from 1-9 (very alert to extremely sleepy, fighting sleep, an effort to remain awake). It has been validated against objective measures of sleepiness using polysomnography, such as EOG slow eye movements, EEG alpha (8–12 Hz) and theta (4–7.9

Hz) activity. The KSS was used daily in connection with the diary every second hour during the day in study I and II to obtain diurnal patterns of sleepiness.

### *Interview*

The interview in study IV was conducted by telephone and was computer-assisted. It consisted of 39 questions in total, this included background information and demographics such as employment and marital status, occupation, health, sleep characteristics and complaints, stress, stress-disturbed sleep, fatigue and impairment of daytime functioning. Prevalence of stress was assessed with the question *“How often have you during the last month felt stressed?”*. Stress-disturbed sleep were assessed with the question *“How often have you during the last month felt that stress during the day have affected your sleep negatively?”*. Answers were given on a scale of 1-5 where 1=never or less than once a month; 2=less than once a week; 3=1-2 times per week; 4=3-5 times per week, and 5=daily or almost daily. The participants were also asked about their health, ongoing medical conditions and burnout (exhaustion disorder): *“Do you have any of the following conditions/symptoms?”*. Answers were given as “yes” or “no”. For assessing causes of sleep disturbances following question was used: *“The times your sleep is disturbed or too short, what is the reason most often?”*. Multiple choices were allowed and the alternatives were: *“stress”, “work/school hours”, “social activities/family and friends”, “small children”, “taking care of a family member (own children excluded)”* and *“use of internet/ phone calls/ text messaging and other technology related activities”*. This was followed by the question *“Of the alternatives you have reported, which one disturbs or shorten your sleep the most?”*. Sleep duration was obtained from the questions regarding average bedtimes and wake-up times on weeknights and days off/ weekends.

Sleep complaints were measured using questions derived from the Uppsala Sleep Inventory (Hetta, Broman et al. 1999) and included questions regarding how often the participants experienced difficulties initiating asleep, difficulties maintaining sleep (repeated awakenings), early morning awakening and non-restorative sleep. Answers were given on a five-point scale based on the frequency with which the different sleep disturbance symptoms was experienced: 1=never or less than once a month; 2=less than once a week; 3=1-2 times per week; 4=3-5 times per week; 5=daily or almost daily. Response alternatives for average number of awakenings during the night was 1=never; 2=once; 3=twice; 4=3-4 times; 5= 5 times or more and for levels of fatigue the alternatives were: 1=no problem, 2=small problem; 3= moderate problem; 4=big problem; 5=very big problem.

## **4.4 STATISTICAL ANALYSES**

All calculations in study I and II were carried out using PASW Statistics 18.0 (SPSS, Chicago, IL, USA) and in study IV with IBM SPSS Statistics, version 24.0. In study II all statistical analyses were performed with the statistical package Stata 11 (Stata Corp, College Station, USA) (StataCorp 2009). Values are expressed as mean  $\pm$  standard error (SE) or number and percentage when appropriate. An alpha level of 0.05 was considered to be of statistical significance.

EEG changes across conditions in study I were analyzed with a repeated measures analysis of variance (ANOVA) using one within group factor: condition (low stress and high stress) and one between group factor (high and low sensitivity to stress related sleep disturbances). For the development of sleepiness, subjective arousal and measures of cortisol a repeated-measures ANOVA was used with time of day as a third factor. When correction for sphericity was needed the Huyhn–Feldt procedure (Huynh and Feldt 1976) was employed. Differences between weekday/ weekend conditions in study II were tested with t-tests.

The main focus in study III was predicting sleep quality from the stress during the preceding day (figure 1), however, since the duration of the previous night’s sleep may affect the following sleep, for certain variables (such as prior sleep quality and TST), the effect of the previous sleep was also analyzed. A multilevel analysis was used for analysis of the longitudinal covariation between variables to handle the two levels, between and within groups, and the serial dependencies of 42 points of measurement (Raudenbush and Bryk 2002). The Stata procedure “xt mixed” was used to estimate linear mixed effect models (Rabe-Hesketh and Skrondal 2005). Missing data were less than 5 %. For evaluation of the effect of individual differences in intercept and slope, a set of linear mixed effect regression models that included a random effect over the intercept in order to allow for variation between subjects, was estimated for all predictors against sleep quality. This was conducted both separately and simultaneously in a multivariate model which reflects the effect of each predictor with all other held constant. Trend across time was controlled for in all analyses. The fixed effects output included a mean regression coefficient ( $\beta$ ) from the individual coefficients, a mean intercept (“constant”) with the Y-axis, the inferential statistic “z”, and p-value. Also, applying random effects allowed for variation of the regression coefficients between individuals and in addition, the intercept with the Y-axis was allowed to vary (“SD constant”). The last random factor was the “SD residual,” that represents the variation around the regression line of each individual.

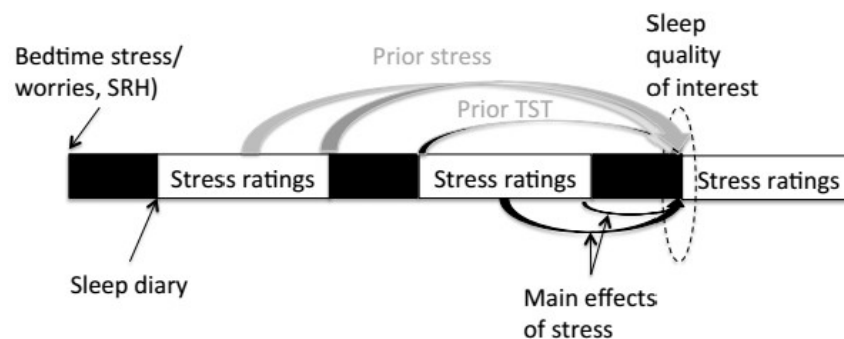


Figure 1. Explanation of the design of the analysis and timing of the measures. The main analysis links ratings of stress during the day and before bedtime to the following mornings ratings of sleep quality. However, ratings of sleep quality and sleep duration (TST) from the sleep the prior night, as well as prior stress, are also used as predictors. Black = sleep; white = wakefulness.

For comparison between categorical and continuous variables in study IV, the chi-squared test and ANOVA was used respectively. Correlations between continuous variables were calculated with linear regression models.

#### **4.5 ETHICAL CONSIDERATIONS**

Studies I, II and III were approved by the ethical committee of the Karolinska Institute, study IV was approved by the ethical committee of Uppsala University. Verbal and written information about the procedures were given for study I, II and III. All subjects were informed that participation was voluntary with the option to terminate participation at any time without further explanation. Before inclusion in the study all presumably healthy individuals were screened and any participant where there was indication of a possible pathological finding have been referred to follow-up in health care. The participants were economically compensated for their time and potential inconvenience. They received 2400 SEK for study I, 3400 SEK for study II, and approximately 1200 SEK for study III. In study IV no economic compensation was given. The respondents received a description of the aim of the survey and then gave verbal consent to participate prior to starting the interview. All participants gave written informed consent before inclusion.

## 5 SUMMARY OF STUDIES

Table 1. Summary of studies

| Study | Title  | N<br>participants | Design  | Measurements  |
|-------|--|-------------------|---|---|
| I     | Stress vulnerability and the effects of moderate daily stress on sleep polysomnography and subjective sleepiness | 36                | Longitudinal<br>Observational<br>Intra-individual (high - low stress)<br>Between groups comparison (high - low vulnerability) | Polysomnography<br>Actigraphy<br>Diary<br>Salivary cortisol |
| II    | Thank god it's Friday – sleep improved   | 17                | Observational<br>Intra-individual (weekday-weekend)   | Polysomnography<br>Actigraphy<br>Diary<br>Salivary cortisol |
| III   | Predicting sleep quality from stress and prior sleep – A study of day-to-day covariation across six weeks        | 50                | Longitudinal<br>observational   | Self-report   |
| IV    | Sleep and stress in Sweden: a population-based survey  | 1128              | Cross-sectional survey<br>Intra-individual (weekday-weekend)<br>Between groups comparison (stress, gender, age)               | Questionnaire   |

### 5.1 STUDY I

The purpose was to study the effects of naturally occurring work stress on sleep during periods of normal and increased levels of stress in 36 teacher's daily life and compare individuals with low and high sensitivity to stress related sleep disturbances.

#### 5.1.1 Method

One week of low work stress and one week with increased levels of work stress was predicted for each participant through weekly web-based ratings of present and anticipated stress. There was no difference in the number of hours worked between the two weeks. During each week one night of sleep was recorded in their own homes with PSG and sleep patterns for the surrounding nights with actigraphy. Sleep characteristics, daytime functioning and perception of sleep quality were measured with sleep diaries. Diurnal patterns of sleepiness and stress were rated every second hour during the days and cortisol was measured through saliva samples collected at 5 times in conjunction with the recording. High and low sensitivity to stress related sleep disturbances were based on the FIRST scale.

#### 5.1.2 Results

Overall, both day and bedtime stress ratings were higher during the period with increased work load and they had more difficulties letting go of thoughts of work. The awakening experience was perceived more negative and daytime cognitive functioning decreased, in

particular for the group with high sensitivity to stress related sleep disturbances. High sensitivity was also related to higher levels of daytime sleepiness during the high stress condition while the opposite was seen among those with low sensitivity. The PSG recording on the night of the high work stress period showed a lower sleep efficiency. The high sensitivity group had less REM sleep and a more fragmented sleep (i.e. more arousals and transitions between sleep stages), while those less sensitive instead showed an increase in REM sleep and had fewer arousals and transitions between sleep stages when work stress was higher. There was no effect of either stress or sensitivity on cortisol levels.

Table 2. Means, standard error of means and F-ratio for sleep variables during high and low stress condition for low and high vulnerability group.

|                   | Low vulnerability |             | High vulnerability |             | F-ratios |       |      |
|-------------------|-------------------|-------------|--------------------|-------------|----------|-------|------|
|                   | Low stress        | High stress | Low stress         | High stress | C        | C x G | G    |
| TST               | 381.8±11.3        | 377.4±10.7  | 441.5±14.7         | 392.2±25.1  | 3.0      | 2.1   | 6.5* |
| WASO              | 31.9±5.4          | 36.7±7.5    | 37.6±9.26          | 52.3±16.7   | 3.5      | .9    | .8   |
| Sleep latency     | 8.2±1.4           | 6.0±1.0     | 8.3±2.3            | 9.6±3.3     | .2       | 2.3   | .7   |
| Sleep efficiency  | 92.5±1.2          | 91.4±1.6    | 92.3±1.8           | 88.7±3.3    | 5.3*     | 1.6   | .3   |
| Awakenings        | 4.2±0.3           | 4.2±0.4     | 3.3±0.26           | 3.8±0.5     | .8       | .67   | 1.6  |
| REM Latency       | 80.9±6.8          | 89.3±7.9    | 114.1±16.0         | 84.4±16.3   | 1.3      | 4.1   | 1.4  |
| SWS Latency       | 32.2±6.3          | 35.2±5.6    | 20.1±2.4           | 19.8±2.9    | .06      | .09   | 3.8  |
| REM               | 91.4±5.4          | 97.0±4.8    | 118.7±7.8          | 92.0±9.0    | 2.8      | 6.4*  | 2.6  |
| Stage 1           | 15.5±2.8          | 12.8±2.2    | 16.9±5.9           | 11.8±1.6    | 2.7      | .3    | .0   |
| Stage 2           | 245.9±6.2         | 240.5±8.5   | 271.3±9.6          | 248.3±21.6  | 1.5      | .6    | 2.5  |
| Stage 3           | 29.0±5.0          | 27.1±4.3    | 34.7±7.2           | 40.0±6.8    | .17      | .7    | 1.7  |
| Stage transitions | 16.3±0.9          | 15.4±0.7    | 14.4±1.1           | 17.2±0.8    | 1.7      | 5.5*  | .0   |
| Arousals          | 6.2±0.5           | 5.0±0.5     | 4.6±0.9            | 5.2±1.1     | .4       | 4.5*  | .5   |

C= Condition (high and low stress), G=Group (high and low vulnerability). Arousals, awakenings and stage transitions are expressed as mean nr per hour of total sleep time (TST). TST, wake after sleep onset (WASO), sleep stages and latencies to sleep stages are presented in minutes, sleep efficiency is expressed in %. \* P<0.05, \*\* P<0.01, \*\*\* P<0.001

### 5.1.3 Conclusion

Periods of increased stress seems to have a moderately impairing effect on sleep and increase sleepiness. However, individual vulnerability to stress disturbed sleep is associated with a greater reactivity.



## 5.2 STUDY II

In this study the aim was to compare objective and subjective measures of sleep characteristics and sleep quality with the sleep of a weekend/ day off with a weekday sleep and investigate if Friday night sleep was followed by lowered stress and sleepiness.

### 5.2.1 Method

From the participants in study I, 17 participants underwent one additional PSG recording in their homes on a night of a workday followed by a day off (Friday), which was compared to the previous low stress sleep registration from study I. The participant's sleep pattern was followed with actigraphy for 2 days in conjunction with the sleep recording, and subjective ratings were reported in sleep diaries. Sleepiness and stress levels were rated every second hour during the day.

### 5.2.2 Results

The self-reported stress levels every 2 hours was lower on the weekend but there were no differences in ratings of stress at bedtime or preoccupation with thoughts of work. On average, the participants slept approximately 45 minutes longer during the weekend, delaying their bedtime with about 30 min in the evening and their time of rising in the morning by approximately 95 min. The weekend sleep was more fragmented than the weeknight sleep, with more awakenings and transitions between sleep stages, and consequently a lower sleep efficiency. Regarding weekend sleep architecture, there was more time in stage 1 sleep, however, it also contained more slow wave sleep (stage 3) compared to the weekday sleep. The final PSG difference found between the two conditions was that the weekend sleep contained less sleep spindles per hour. As described in the introduction the architecture of sleep changes with sleep duration, for example, towards the end of sleep there is an increase in REM and slow wave sleep decreases. Because the two sleeps had different lengths, the morning hours of the weekend sleep were truncated to match the duration of the workday sleep. The smallest common denominator from bedtime of both sleeps was 5 hours, and thus only the first 5 hours of both sleeps were analyzed again. The difference in SWS and stage 1 remained, and in addition there was a significant decrease in stage 2 and REM sleep. The truncated weekend sleep still contained less sleep spindles and more stage transitions, but the increase in awakenings per hour disappeared. The simultaneous increase seen in stage 1 and stage 3 sleep during weekend sleep was unexpected, therefore we also computed correlations between the change in all NREM sleep stages. Results revealed a positive correlation between the increases in stage 3 and stage 1 sleep ( $r = 0.849$ ,  $P \leq 0.01$ ) and a negative correlation between the decrease in stage 2 and the increase in stage 3 ( $r = 0.660$ ,  $P \leq 0.01$ ) as well as to the increase in stage 1 sleep ( $r = 0.696$ ,  $P \leq 0.01$ ). Subjective sleep quality did not differ between weekday and weekend, but the awakening experience was significantly better during the weekend.

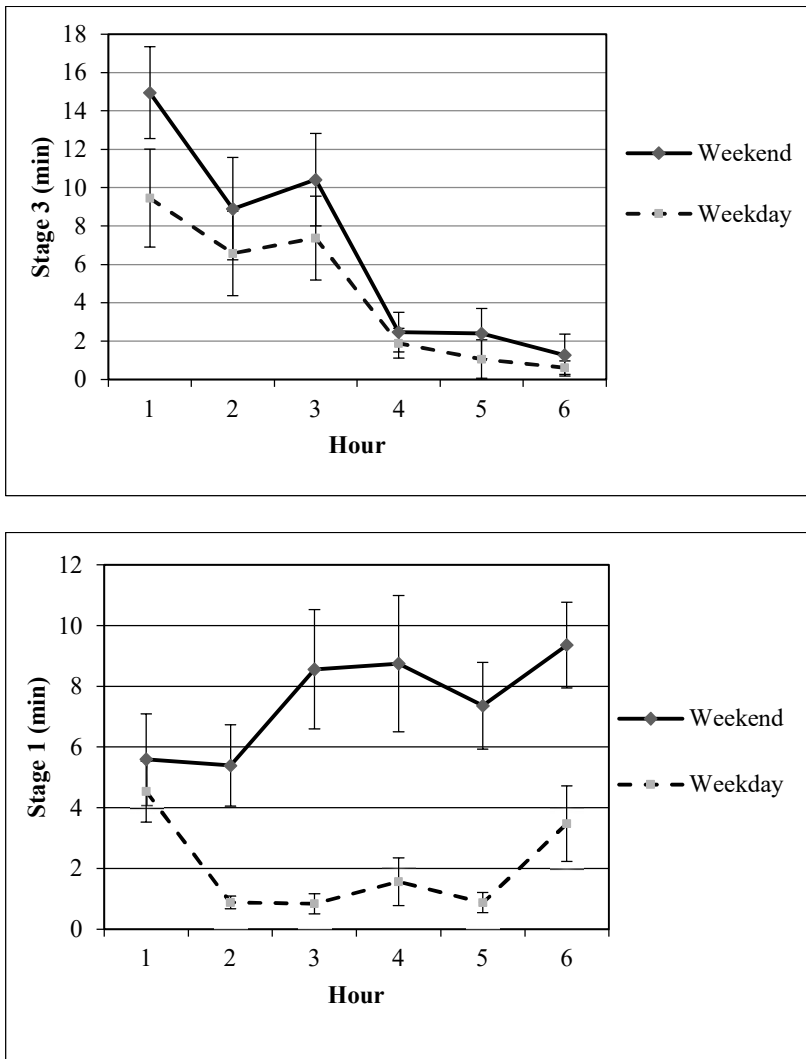


Figure 2. Mean minutes and standard errors of stage 3 and stage 1 sleep per hour of weekdays and weekends.

### 5.2.3 Conclusion

Weekend sleep was characterized by delayed bedtimes and time of rising in the morning, and sleep duration was increased but more fragmented. Architecturally, weekend sleep contained more stage 1 and 3, while stage 2 and REM sleep decreased. There seems to be an improvement in sleep during the weekend compared to the weekday sleep regarding amount of slow wave sleep and waking up feeling more restored and rested, possibly as a result of lower stress levels due to anticipation of a day off.

### 5.3 STUDY III

In this study we examined how different levels of stress from day-to-day relates to the day-to-day variation in sleep quality. It was hypothesized that stress during the day and evening would result in next morning reports of poor subjective sleep quality.

#### 5.3.1 Method

Over a period of 6 weeks, 50 participants filled out the Karolinska Sleep Diary (Akerstedt, Hume et al. 1997). Every evening they reported their mood, health, and different indicators of fatigue and each morning they rated their sleep quality and reported on bedtimes, sleep characteristics, the awakening experience and factors that might affect sleep (e.g. coffee, alcohol etc.). Sleep quality was measured with a sleep quality index (SQI) formed by four questions; *‘how did you sleep?’*, *‘calm sleep’*, *‘ease of falling asleep’* and *‘slept throughout the allotted time’* rated on a scale of 1-5 (very good 5 – very poor 1). Stress was rated every 3 hours on a scale from 1-9 (none 1 - maximum stress 9) during the day for the entire study period and *‘stress/worries at bedtime’* every evening on a scale from 1-5 (none 5 - very much 1). A measure of burnout was obtained using the Shirom-Melamed burnout scale (Melamed, Kushnir et al. 1992). A multilevel analysis was used to analyze the longitudinal covariation between the variables. The main focus was the prediction of sleep quality from stress and other variables during the preceding day, but also the influence of sleep quality and duration of the sleep episode prior to the day.

#### 5.3.2 Results

Stress/worries at bedtime was the main predictor, with a decrease of 0.3 units in subjective sleep quality with every 1 unit increase of stress/worries. This was followed by time of awakening, where every hour of later awakening yielded a change of 0.05 units increase in sleep quality. Also, there was a lagged effect of both sleep duration and sleep quality of the previous night: Longer prior sleep duration was connected to a reduction of sleep quality. Additionally, self-rated health was associated with increased quality of the upcoming sleep. For stress/worries the variation between individuals was similar to the fixed effect, indicating a rather stable effect between stress and sleep quality among individuals, while the other predictors displayed a considerably higher random effect and less stable relationship. Repeated ratings of stress during the day were associated with poorer sleep quality in univariate analysis but that association disappeared when analyzed together with stress/worries at bedtime. Among the background variables included as possible modifiers, only depression and anxiety were significant in the multivariate analysis. Both showed an association with reduced sleep quality. Considering the possibility of bidirectionality, the predictive value of previous sleep episode on stress ratings the following day was also analyzed. Results showed an increase of 0.08 units of stress/worries at bedtime for each unit of sleep quality decreasing.

### 5.3.3 Conclusion

Sleep quality seems to be quite sensitive to modest variations in daily stress and was most strongly predicted by the level of stress before going to bed. The higher the stress, the poorer the sleep. Since the effect of stress during the day was much weaker than that of stress at bedtime, it seems likely that the link between stress/worries at bedtime and sleep may be caused by an anticipation of problems the upcoming day. Other factors affecting day-to-day variations in sleep quality is the time of awakening from the prior sleep, and perceived health.

## 5.4 STUDY IV

The objective of the final study was to examine how disturbed sleep is attributed to stress and other causes and how stress relates to specific aspects of disturbed sleep as well as sleep duration on both weekdays and weekends in a nationally representative sample. Another objective was to study the association of stress and stress disturbed sleep to age and gender.

### 5.4.1 Method

The sample was randomly selected, representative for the Swedish population and proportionally stratified for age and gender. In total, 1128 participants between the age of 18-84 years completed a computer-assisted telephone interview. The interview consisted of 39 questions regarding sleep patterns, sleep complaints and stress and included demographic background information such as occupation, age and marital status. The questions assessed prevalence of stress and stress disturbed sleep during the last 4 weeks, answers were given on a scale of 1=never or less than once a month - 5=daily or almost daily. They were also asked which causes they attributed their disturbed sleep to most often. Alternatives were: *stress, work/school hours, social activities/family and friends, small children, taking care of a family member (own children excluded) and use of internet/ phone calls/ text messaging and other technology related activities.*

### 5.4.2 Results

Stress was the most common cause of sleep disturbance, reported by about 35% of the participants. Other commonly reported causes were work/ school hours (15.9%), social activities/family and friends (13.3%) and small children (12.8%). Women especially attributed more sleep disturbances to stress than men, and it was also more common in younger people. In the older group the most frequently reported causes following stress was personal health and social activities/friends and family, and in the younger group it was work hours and small children. Use of internet, mobile phone or other technology related activities was more common among men. The average frequency of stress was approximately 1 day per week and of stress disturbed sleep a few days/months. Overall, about half of the women and 38 % of the men reported experiencing some degree of stress. Very frequent stress, 6-7 days of the week, was reported by 12.3 %. About a third of those individuals with a prevalence of stress 3 or more days of the week also reported problems with stress related sleep

disturbances 3-7 nights per week. Women had a higher frequency of stress and stress disturbed sleep than men. Frequency of stress followed the same pattern in both genders, slightly increasing from upper teenage years to a peak in the 35-44 years age group and then declining with higher age. The pattern for stress disturbed sleep was similar to that of stress but with the peak occurring in the 45-54 years age group. The individual sleep items most related to stress was those representing a lack of restoration; insufficient rest from sleep, too little sleep, and fatigue. For those reporting low to moderate stress (0-5 days/week), sleep duration on weekdays decreased with increased stress frequency while the weekend showed an opposite relationship (figure 4). However, among those with frequent stress (>5 days/week), sleep duration for both weekdays and days off was reduced.

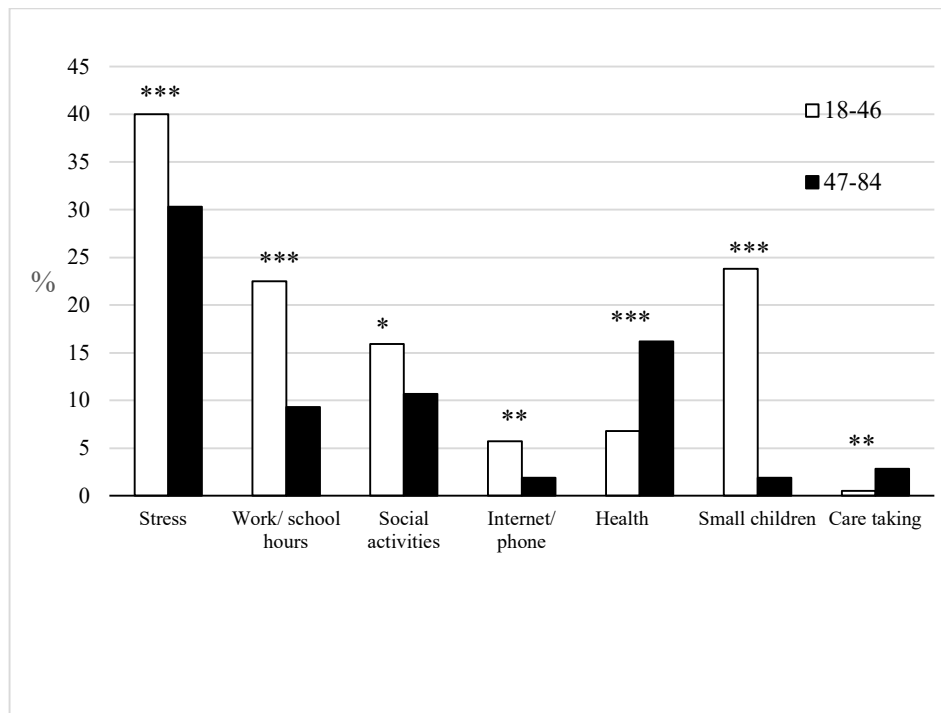


Figure 3. Causes of disturbed sleep in % of age groups 18-46 years and 47-84 years. \*\*  $p < .01$ ; \*\*\*  $p < .001$

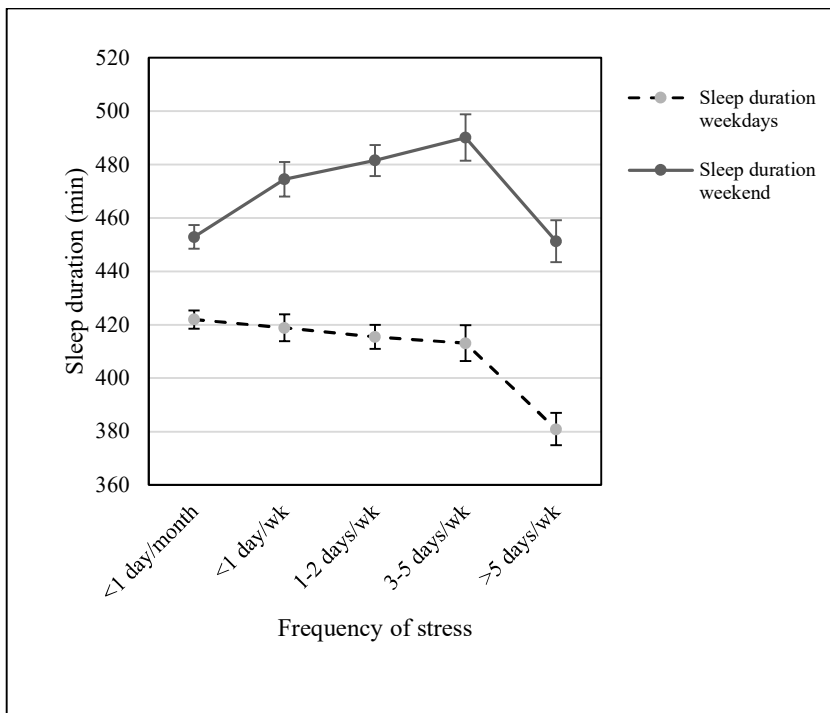


Figure 4. Means and standard error of means for sleep duration related to stress frequency on weekdays and weekend.

### 5.4.3 Conclusion

Prevalence of stress and stress disturbed sleep was higher in women and it was also more common for younger people. Stress was the most common cause of disturbed sleep, followed by work hours, and women in particular attributed many of their sleep disturbances to stress. The specific symptom of disturbed sleep that was most related to stress was non-restorative sleep. Sleep duration for weekdays and weekends was reduced among those with frequent stress.

## 6 GENERAL DISCUSSION

The overall aim of this thesis was to examine the relationship of naturally occurring, day-to-day stress and sleep. More specifically, how different intensity of real-life stress affects both objectively measured sleep and perceived sleep quality, as well as the role of individual vulnerability to stress-disturbed sleep. In addition, we aimed to examine the prevalence of stress, stress-disturbed sleep and the causes sleep disturbances are attributed to in the general population. This was investigated through three studies that support the notion that stress predicts poor sleep and one study that identifies stress as the main reported cause of disturbed sleep.

### 6.1 HOW DOES STRESS AFFECT SUBSEQUENT SLEEP?

#### *Objective sleep quality (PSG)*

The main difference between high and low work stress was seen in sleep efficiency which was significantly decreased during the high stress condition (high stress 90.1 % and low stress 92.4%). Previous studies have found similar results, for example in a study by Åkerstedt et al (2007), where days with higher rated stress was followed by a night of reduced sleep efficiency and increased fragmentation. In that study they also found the sleep related to high stress to contain more wake time, which we also saw a trend towards in study I, although not statistically significant. However, in many key indicators of sleep quality (i.e. sleep duration, sleep latency, SWS and REM sleep), no significant associations were found.

There are unfortunately not that many PSG studies of naturally occurring stress to compare with, but the reduction in sleep efficiency and increased sleep fragmentation was also seen in two studies on burnout, both working individuals (Söderström et al., 2004), and those on sick leave (Ekstedt et al., 2006). The latter study had large effects and there was also a reduction of both SWS, REM sleep, latency to REM sleep and a longer general latency to sleep. Apart from the reduced SWS, the other PSG changes in that study disappeared after recovery and can thus be linked to higher stress levels. An effect on REM sleep was seen in study I as well, but in different directions depending on habitual stress reactivity which will be discussed further below in relation to individual vulnerability to stress-disturbed sleep.

In comparison between a week with normal levels of work stress, and a sleep after a workday followed by a day off (intended to reflect a stress-free sleep), the Friday sleep was longer and contained more SWS, which was interpreted as an improvement from weekday (stress exposed) sleep. As daytime stress levels were lower, which was also seen in previous weekend sleep study (Söderström et al., 2004), it seems likely that the increase in SWS was due to participants relaxing before a day off. There was a trend ( $p = 0.055$ ) on the day of the weekend sleep, indicating a more positive anticipation of the following sleep which would

support this assumption. But there was also the unexpected result of an increase in stage transitions and stage 1 sleep which typically indicates a lower sleep quality (Rosipal, Lewandowski et al. 2013) (Åkerstedt, Hume et al. 1997). SWS is generally considered to have the most recuperative value (Åkerstedt, Hume et al. 1997) (Dijk, Groeger et al. 2006), however, increased SWS is also found as an effect of sleep loss, although usually accompanied by less sleep fragmentation and stage 1 sleep (Borbély, Baumann et al. 1981). This could be interpreted as an impairment of weekend sleep, but as the change in stage 1 and stage 3 sleep positively correlated to each other, it rather appears that there is a common factor causing them to increase together. A clear logical explanation of this finding is difficult to produce, but it is possible that its connected to the reduction found in sleep spindles. A reduction in sleep spindles along with increased SWS have previously been shown in studies of recovery sleep (Curcio, Ferrara et al. 2003) (Achermann, Finelli et al. 2001). Sleep spindles are a non-REM sleep characteristic, most frequently occurring in stage 2, while stage 3 contains fewer sleep spindles (Rechtschaffen and Kales 1968). Therefore, a reduction in spindles can be expected as a direct effect of less stage 2 and more stage 3. A possible consequence of the lower number of sleep spindles, is that more epochs of sleep would be scored as stage 1, instead of stage 2.

Taken together, Study I and II, as well as the studies by Åkerstedt et al (2007) and Söderström et al (2004) show rather modest effects of stress on polysomnography. This is in contrast to the pronounced effects seen in Ekstedt et al (2006). The difference may be that the latter study investigated individuals with a long-term exposure to stress and on sick leave for burnout (exhaustion syndrome), and with high values on the burnout scales, as well as the scales for sleep disturbances. That is, levels of stress (which was not formally rated) must be considered very high. The first four studies, on the other hand, seem to have investigated more modest stress levels (see also discussion below).

### *Subjective sleep quality*

When it comes to sleep quality, as discussed in the introduction, it is not entirely clear or easy to define what good sleep means objectively. From the results of study I it would seem that the impairment of sleep caused by high stress mainly consisted of a disruption of continuity, which presumably would manifest in subjective perceptions of poor sleep the next morning. The participants did however not rate their overall sleep quality as much lower after high stress. Instead, what did show a clear impairment was in how they rated their awakening experience (or restorative sleep (Stone, Taylor et al. 2008)). The awakening index is comprised of questions on difficulties awakening, feeling refreshed by the night's sleep and on the sleep being sufficient. This seem to reflect a feeling that the sleep of that night was not sufficient enough to give a complete recovery. One explanation could be that the higher level of stress increased the need for sleep, a need which might have been possible to meet had they been able to extend their sleep duration. In the present study there was a trend ( $P < 0.10$ ) towards shorter sleep during high stress. This is however probably not useful to compare,



since both sleeps were subject to the similar time constraints, that is the work hours. However, the group that was more sensitive to stress had a longer TST than the less sensitive, this would support the idea of a greater need for sleep. This lack of recovery from sleep was also reflected in an increased sleepiness the following day, which was seen in the participants classified as more sensitive to stress disturbed sleep. Even though there was no significant difference in TST between high and low stress conditions, there is a clear association of sleep fragmentation and higher level of sleepiness (Stepanski, Lamphere et al. 1984) (Bonnet and Arand 2003) so it is reasonable to think that the higher number of arousals and stage transitions could explain this finding.

Other indicators of the high stress sleep being less recuperative were the ratings showing reduced daytime functioning and feeling less healthy. In study IV it was the sleep symptoms that represented non-restorative sleep that was most connected to stress in the general population, which has been found to be the most common symptom of sleep disturbance in other population-based studies, experienced by as much as 18 % of the population (Ohayon and Bader 2010). The finding in study III, that a late awakening was associated with higher perceived sleep quality, is also in support of the assumption that it is the perceived recuperative value of sleep upon awakening that is most important regarding perception of sleep quality, and that it is in fact the consequences of sleep disturbances that mainly influence that perception rather than the disturbed sleep in itself. This is consistent with the results of Åkerstedt et al. (2016) where the sleep symptoms that were observable by the participants in the morning were those mostly related to subjective sleep quality (Åkerstedt, Schwarz et al. 2016). The definition of insomnia also reflects this as it includes restoration in addition to difficulties falling asleep and disrupted sleep (AASM 2014). Daytime functioning demands, as reflected in the ratings of cognitive functions, sleepiness and mood, may presumably be experienced as lighter if there is opportunity and ability to extend sleep. However, study III also showed that a longer TST the night before led to decreased sleep quality for the upcoming sleep. This is probably more related to a change in homeostatic sleep pressure which would lessen the need of recovery (Borbely 2009).

### *Stress and subjective sleep quality*

For the question of whether stress predicted subjectively poor sleep, the hypothesis was that higher perceived stress in the evening before bedtime would lead to poorer subjective sleep quality as reported in the morning. There is undoubtedly a high correlation between stress and sleep as evidenced in previous research (Garefelt, Platts et al. 2019), stress have been linked to sleep quality in numerous longitudinal (Morin, Rodrigue et al. 2003), cross-sectional (Urponen, Vuori et al. 1988) (Ancoli-Israel and Roth 1999) (Utsugi, Saijo et al. 2005) (Åkerstedt, Fredlund et al. 2002), and prospective (Ribet and Derriennic 1999) (Linton 2004) (Jansson and Linton 2006) (Åkerstedt, Kecklund et al. 2007) studies, it seems however reasonable that not all stress automatically leads to sleep disturbances as the results of study IV showed where just under 9 % of the participants reported having stress disturbed sleep at

least 3 days of the week while more than twice as many (22.2%) had experienced stress of the same frequency. When looking at the chronically stressed individuals (defined here as reported average occurrence of stress 6-7 days of the week) the proportion who also had chronic stress-disturbed sleep was a third. Based on the results of study III, an important factor in the link between stress and disturbed sleep seems to be the timing of stress. It was found that ratings of stress at bedtime showed a much stronger connection to poor sleep than did the ratings of stress during the day. Even though the univariate analysis showed that higher mean ratings of stress during the day were significantly related to poorer quality of sleep the following night, this relationship was no longer statistically significant in the multivariate analysis with other predictors, as the impact of bedtime stress and worries were much greater. This may reflect that the bedtime stress summarizes the combined effect of the day's stress, and that stress during the day causes arousal at bedtime as suggested by Morin et al (Morin, Rodrigue et al. 2003). It could also indicate that stress during the day does not have a large effect on sleep unless the stress level is maintained up to the time of going to bed. Another possible mechanism could be the anticipation of stress in some form the following morning or day. It has previously been found that for example individuals with occupations that requires very early morning wake up (Kecklund, Åkerstedt et al. 1997) or a duty to be on call during the night (Torsvall, Kastenfors et al. 1987) have shown impaired sleep in response.

The connection between stress and sleep quality showed much stronger effects in study III than in the two PSG studies. Although one cannot compare objective and subjective measures directly, it raises the question whether it is possible to capture the true effect of naturally occurring stress on objective sleep. Data from diaries and web-based questionnaire show that stress was higher during the high stress condition sleep recording. Stress ratings at bedtime were also higher, which the results of study III suggest is most important for sleep, at least in terms of perceived sleep quality. Still, the effects were not as large as expected, in contrast to a previous study where the high and low stress conditions were selected from ratings after a number of sleeps had been recorded weekly (Åkerstedt, Kecklund et al. 2007). One reason could be that the low stress was not low enough, as teachers are one of the occupations reporting the most stress. There may be a longer period of relaxation needed to discover larger differences between conditions. Type of stress could also come into play, if the stress involved mainly an increased work load, without any lingering emotional components such as anticipatory stress and worries (Harvey 2002), it may not disturb sleep as much. For example, in a study by Åkerstedt, Nordin et al (2012) it was found that inability to psychologically detach from work thoughts predicted sleep disturbances to a higher extent than work demands did. It may be possible that had the stress condition in study I involved a higher level of work-related rumination, then the differences in PSG-assessed sleep had been more pronounced. The participants were school teachers, an occupation deliberately chosen because periods of higher job-strain and stress can be assumed to be frequently occurring aspects of the teaching profession. Thus, if the periods of higher stress are reoccurring at given times during the school term, they may be better mentally prepared for it as opposed to

for example an unexpected increase in work load due to organizational changes, and therefore less impacted in terms of preoccupation with thoughts of work.

Another explanation could lie in the absence of effect on cortisol levels during high stress in study I. Cortisol has previously been linked to sleep fragmentation in people with high ratings on burnout (Ekstedt, Åkerstedt et al. 2004), indicating that the stress in study I might not have been of the type or of an intensity high enough to cause a sustained activation of the stress response and consequently the impact on physiological sleep was lower.

An important observation is that the variation of both stress and sleep quality were restricted within a rather modest dispersion. Average sleep quality of the participants in study III was above the population average and the levels of stress/worries were confined to the lower end. One might assume that the effect had been larger if the distribution of the two variables had been wider. It also indicates that reported sleep quality has a rather high sensitivity to even small variations in level of stress. As for causation, although there was an effect of poor sleep predicting upcoming stress, the effect in that direction was modest and the results seem rather to add credibility to and support previous implications of a causal stress-to-sleep connection.

### **6.1.1 Effects of stress on sleep duration**

In both study II and IV we saw significant extensions of PSG-assessed and self-reported sleep duration during the weekend, compared to weekdays. This difference was expected as longer sleep on weekends have been reported in several population-based surveys (Groeger, Zijlstra et al. 2004) (NSF 2002) and in line with previous similar observations (Basner, Fomberstein et al. 2007) (Söderström, Ekstedt et al. 2004). It is however difficult to say whether the extended sleep duration is an effect of less stress or just having the freedom to choose and possibility of extending sleep. One would have to include a workday with a later start to know how long they would sleep after exposure to work stress if they were free to wake up at their own desired time on weekdays as well. With respect to stress however, there appeared to be a compensation during the weekend associated with higher stress and decreased sleep time during the weekdays. Shorter sleep on weekdays have previously been associated with stress (Knutson, Phelan et al. 2017) (Dahlgren, Kecklund et al. 2005) but there is not a lot of data on weekend compensation related to stress induced sleep reduction during the week to compare with.

An interesting observation in study IV was that among those that reported stress on a chronic level, that is 6-7 days of the week on average, sleep duration was shorter not only on weekdays but also on the weekend. This was not in line with the pattern we saw of weekend sleep compensation related to higher stress and reduced weekday sleep duration. One may speculate that such high frequency of stress, involving maintained stress levels on at least one day of the weekend and for some the whole weekend, could prevent any possibility to recover the accumulated sleep loss. A long-term situation with chronic high stress levels without the relief of sufficient recovery sleep may easily turn into a vicious cycle. Prolonged stress is known to have a negative impact on recovery (Åkerstedt 2006) (Sonnentag 2018), and

research shows that when daytime and evening recovery is hampered, it may increase the risk of sleep disturbances (Tucker, Dahlgren et al. 2008). The impaired sleep may then in turn lead to increased negative affect, a factor that may further reduce the ability to recovery (Sonntag, Binnewies et al. 2008).

We did not have data on whether the weekend included work that limited the sleep hours reported in study IV and thus it is not possible to say whether the sleep was shorter during the weekend due to voluntarily restricting sleep or as a result of stress interfering with sleep. In an experimental study where healthy subjects over the course of three weeks restricted their weekday sleep to 4 hours which were followed by two nights of 8-hour sleep during the weekend (Simpson, DiIombi et al. 2016), the researchers saw a dysregulation in several physiological markers of stress, such as cortisol and glucocorticoid receptor sensitivity. But perhaps most importantly, they made the interesting observation that despite the obvious activation of the physiological stress response, the sleep restriction in itself were not perceived to be stressful by the participants. The authors suggest that this dissociation partly explains why voluntary sleep restriction due to for example work hours is so commonly continuing for longer periods of time. It seems unlikely however that all the individuals with chronic stress levels in study IV would be working every weekend. A more likely explanation, although speculative, is that the inability to extend sleep on the weekend is related to the fact that this group reported a higher prevalence of several health-related issues, in particular on burnout symptoms. Studies on burnout have shown that individuals with high scores on burnout, both on sick leave (Ekstedt, Söderström et al. 2006) and those still working (Söderström, Ekstedt et al. 2004), have impaired sleep, but also an impaired ability to recover on days off.

## **6.2 TRAIT ASPECTS OF SLEEP VULNERABILITY TO STRESS**

In study I we were also interested in whether sleep after high stress was more affected in regard to PSG in individuals that were self-reportedly more prone to react to stress with disturbed sleep. We used the FIRST scale (Drake, Richardson et al. 2004) to classify individuals as either belonging to the high sensitivity or low sensitivity group in terms of how they normally respond to situations they perceive as stressful.

That the group with a pre-existing high sensitivity to stress had poorer subjective sleep was quite expected, as they themselves reported often experiencing disturbed sleep in different situations deemed stressful, but that may not necessarily mean that objective measures of sleep would show impairment. Apart from the overall reduction in sleep efficiency both groups had during high stress, PSG measures showed that the individuals with high sensitivity to stress-disturbed sleep reacted with a higher degree of sleep fragmentation and reduced amount of REM sleep compared to the sleep that was recorded during a week with lower levels of work stress. This is in accordance with a previous study on individuals on sick-leave due to burnout, where both amount of REM sleep and latency to REM sleep was significantly reduced (Ekstedt, Söderström et al. 2006). Reduced, fragmented and in other ways altered REM sleep seems to be a reoccurring theme related to stress, it has been seen in

connection to several different psychiatric conditions as well, such as post-traumatic stress disorder (Baglioni, Nanovska et al. 2016) (Yetkin, Aydin et al. 2010). Although results from human sleep studies are mixed (Akerstedt, Kecklund et al. 2007) (Pillai and Drake 2014) (Vandekerckhove and Cluydts 2010), animal studies have shown a connection between high vulnerability to stress and REM instability, i.e. reduced duration and increased fragmentation of REM (Pawlyk, Morrison et al. 2008) (Fenzl, Touma et al. 2011) (Revel, Gottowik et al. 2009).

According to the stressor reactivity model (Bolger and Zuckerman 1995), when exposed to perceived stressors, individuals differ in the extent to which they are likely to express stress reactions. It has been suggested that once a person has reached the stage of exhaustion, then that person could develop a higher sensitivity to additional stress and even become less tolerant to minor stressors (Besèr, Sorjonen et al. 2014). Exactly what makes some individuals more resilient and some more vulnerable to stress is not known, but both genetics (Franklin, Saab et al. 2012) and behavioral patterns like self-efficacy (Bandura 1982), coping (Lazarus 1993) and over-commitment (Siegrist 1996) plays in. There are also other risk factors such as financial strain (Thoits 2010) and work-family conflict which has been found to be a major stressor, particularly for women (Leineweber, Baltzer et al. 2012). These are factors that were not addressed in the study and thus unaccounted for, but since the majority of the teachers were women, especially the potential role of work-family conflict would be interesting to include as a mediator in future studies.

### **6.3 ATTRIBUTED CAUSES OF DISTURBED SLEEP**

The question whether stress is seen as a major sleep disturber was addressed in study IV, and it showed that it clearly was in the general population, reported by 35 %. It was by far the cause people most often attributed their disturbed sleep to, more than twice as common as work or school hours which came in second. From the correlative studies previously discussed (Akerstedt, Nordin et al. 2012) (de Lange, Kompier et al. 2009), the finding of stress as the main cause of disturbed sleep was expected, these results however establish this in a nationally representative sample. Work hours is also an established cause of sleep disturbances (UNISON 2017) and was expected as well to be reported by a high proportion of people. In the two first studies stress caused a mild acute sleep disturbance and it seemed reasonable to assume that the extended sleep on the weekend was a way of recovering some of the lost sleep accumulated during the week. In that aspect, work hours may be seen as a contributing factor to stress as a sleep disturber, since the possible harmful effect on health caused by stress in form of sleep fragmentation and reduced sleep efficiency might be possible to reverse by extending sleep. It is however not possible to know if the attribution of sleep problems to work hours in this study was in connection to, or in absence of stress. The participants were asked which was the most common sleep disturber, and in hindsight it is unfortunate that the phrasing of the question did not allow for any combinations of causes which may have been present.

Consistent with previous reports of women having more stress (AXA 2018) (Klein, Brähler et al. 2016), there was a significantly higher attribution of disturbed sleep to stress among women, but otherwise there were no large gender differences in attribution. The frequency of stress disturbed sleep was also higher in women. An explanation may be that women and men have different ways of managing and responding to stress. In a study by the American Psychological Association almost half of the women, 49 %, reported lying awake at night as a consequence of stress (American Psychological Association 2010) and similarly, a British national survey found that women were more likely to extend their bedtime and be preoccupied by their problems because of stress (AXA 2018). Thus, a probable contributing factor in explaining the gender differences in stress-disturbed sleep is that women tend to ruminate more than men (Tamres, Janicki et al. 2002) (Johnson and Whisman 2013).

Younger people attributed more of their sleep problems to stress, as well as the majority of causes. A plausible reason for this could be that they are more likely to be either in the beginning or middle of their careers, with higher prevalence of work-related stress and more often having disadvantageous work or school hours (SCB 2018), some maybe even combining work with school studies. Younger people are also likely to being more frequent users of smartphones, internet and other technology related activities, which may increase daily stress levels (Thomee, Harenstam et al. 2012).

#### **6.4 ASSOCIATION BETWEEN AGE AND STRESS-DISTURBED SLEEP**

This question was addressed in study IV. In regard to frequency of stress, we saw a decline with age that was expected from previous research (Akerstedt, Discacciati et al. 2019). There are many plausible explanations for this, such as decreasing demands from work (Akerstedt, Discacciati et al. 2019) or absence of work demands altogether as a consequence of retirement (Vahtera, Westerlund et al. 2009). Interestingly, the effect size for age as a predictor of stress was considerably larger than that of gender, suggesting that age has a stronger connection to stress even though it is well-established that women consistently report more stress than men (AXA 2018) (Klein, Brähler et al. 2016).

The results also showed that stress disturbed sleep was less frequent in older individuals, which does not seem to have been reported before, to the best of our knowledge. There are however studies supporting the connection between age and stress disturbed sleep found here, for example the study by Johnson et al (Johnson, Lisabeth et al. 2016) which found that stress was negatively associated with both sleep quality and the duration of sleep and that these effects were stronger for younger people. This may be directly related to the above mentioned here and otherwise reported decrease in stress with older age (Akerstedt, Discacciati et al. 2019), although sleep problems interestingly seem to increase with age (Akerstedt, Discacciati et al. 2018). On the other hand, there have also been indications of a higher tolerance for sleep disturbances with increasing age (Akerstedt, Schwarz et al. 2016). For example, older individuals have been found to tolerate sleep deprivation better than younger in terms of effect on cognitive functions and sleepiness (Philip, Taillard et al. 2004) (Duffy, Willson et al. 2009).

An alternative explanation is the “positivity effect” (Reed and Carstensen 2012), which refers to age-related changes in emotion regulation, that is, older people in general tend to prioritize positive information over negative (Reed, Chan et al. 2014). This age difference in emotional stimuli processing has been confirmed in brain imaging findings (Mather 2012). For example, Schwarz et al (2019) found that older participants showed a dampened increase in negative mood to sleep deprivation compared to younger participants, despite similar levels of sleepiness (Schwarz, Axelsson et al. 2019). However, this age-related normally dampened response to negative stimuli were shown to be less pronounced during a stressful situation (Everaerd, Klumpers et al. 2017).

In the same way as retirement may be a large factor in the age-related decline in stress mentioned above, it may partly explain the lower prevalence of stress-disturbed sleep. For people that have retired from work there are likely fewer daytime demands of concentration, being focused, keeping appointments or physical workload etc. that the effects of sleep loss or sleep disturbances can interfere with. Effects of poor sleep may be ignored if they don't cause any problems for the individual – hence not seen as a sleep problem. Older age also means that they are less likely to have small children living at home. In a similar way as being retired from work, it may allow for a bigger flexibility in choosing one's own bed- and waketime. It is also possible that one reason older people report less stress related sleep disturbances than younger people is that they consider disturbed sleep a natural consequence of older age and therefore does not discern between other possible causes in the same extent as younger people who might have higher expectations on their sleep quality. Many of the changes that naturally accompany age, such as a reduction of sleep duration and SWS (Mander, Rao et al. 2013) (Dijk, Groeger et al. 2010), as well as a reduced strength of the circadian signal and the homeostatic drive for sleep (Dijk, Duffy et al. 1999), are aspects of sleep commonly associated with poor subjective sleep quality. Additionally, older adults have been found to more often seek medical advice about sleep, have a diagnosed sleep disorder and use sleep medication (Knutson, Phelan et al. 2017) which may indicate that they are more accepting of sleep disturbances as an inevitable part of aging as opposed to a temporary consequence of stress. Further, Åkerstedt et al, (2016) (Åkerstedt, Schwarz et al. 2016) found that the perception of sleep quality changes with age. For example, older women's self-rated good sleep consisted of shorter sleep duration, lower sleep efficiency and more WASO than what the younger women needed to rate their sleep as good. Also, the polysomnographic measures of the sleep that older people rated as being of good quality was similar to those of poorly rated sleep in younger individuals. However, it could also be that people of older age do not need as much sleep and as high quality of sleep as younger people to feel rested, as several studies have shown that daytime sleepiness and fatigue, which likely affects perceived restitution of sleep, decreases with age (Dijk, Groeger et al. 2010) (Åkerstedt, Discacciati et al. 2018). This could hypothetically mean that the prevalence of objectively stress-disturbed sleep may be higher than the subjectively perceived prevalence that was reported.

## 6.5 STRENGTHS AND LIMITATIONS

The main strengths of the first three studies include the within-individual variation and that the data was collected in naturalistic conditions (emphasizing ecological validity). An additional strength is the considerable amount of data points in study III, which consisted of 50 individuals and 42 days of ratings, providing well over 2000 ratings. However, the study samples of the first three studies were relatively small, meaning that the statistical power for between-group variation was lower and that small effects were difficult to detect. Also, in study I and II there was only 1 sleep recording per condition, the inclusion of more sleeps would of course have improved the accuracy and taken the intra-individual variability among the participants in account.

The fact that the data collections took place in the participants home environment can also be a limitation as there are many external/unmeasured factors that may affect the results and which could have been controlled in a laboratory setting. On the other hand, a key point in the study was to observe effects of stress and sleep in a natural environment with as little deviation as possible from the participants normal routines. Another limitation of study I was the use of a modified version of the FIRST scale. In order to better suit the purpose of studying effects of work stress, it was deemed important to add items about work stress situations. to the original scale. This means that previous validation work of the original FIRST scale cannot be readily applied. On the other hand, the modified version of the scale had a high Cronbach alpha (0.87) and was successful in predicting differential PSG responses to stress.

The biggest strength of study IV is the population-based nationally representative sample with a broad age-range and a response-rate that was very high (72,8%). An additional strength is that, to the best of our knowledge, this is the first nationally representative study conducted in Sweden investigating the causes of disturbed sleep. Being a cross-sectional study, data collection was made at one point in time, and this point happened to be in the month of December. This could potentially affect the results considering that it is the darkest month of the year in Sweden and there is a documented effect of sunlight exposure on sleep (Dumont and Beaulieu 2007) (Düzgün and Akyol 2017). Another temporal factor that could possibly lead to an overestimation regarding the prevalence of stress is the effect of the Christmas holiday. Several stress-related conditions increase during the holiday season, such as mood disorders and cardiac morbidity and mortality, (Sansone and Sansone 2011) (Mohammad, Karlsson et al. 2018) (Knight, Schilling et al. 2016). All interviews took however place during the same month, thus eliminating the risk of any seasonal differences between groups.

Data in study I and IV were limited to self-reports, however, that is a common procedure with evaluation of stress. With regard to both stress and sleep quality this may not be a problem as diagnoses of for example insomnia (Edinger, Bonnet et al. 2004) and burnout (Korczak, Huber et al. 2010) are normally based on subjective reports. An advantage of using subjective measurements is that it allows for taking individual differences in vulnerability into account,



but self-ratings also carry a risk of inaccurate perception or misinterpretation of the questions. A related risk is participant recall bias (Coughlin 1990). Accuracy would very likely have improved if a shorter recall period had been used than the 4 weeks that were the case in study IV, but on the other hand that would have limited the day-to-day variance. One important limitation regarding all studies is the possibility that chronically stressed individuals, or those who's sleep responds the strongest to stress tend not to take part in the studies, as they may feel that participation would add a considerable stress burden or disturb their sleep further, i.e. similar to the healthy worker effect (Shah 2009).

As previously discussed, stress can have consequences for sleep, and poor sleep can be a stress load in itself (Soderstrom, Jeding et al. 2012) (Sonnentag, Binnewies et al. 2008). Thus, when interpreting the results, the problem of reversed causation must be considered (Kahn, Sheppes et al. 2013), i.e. whether stress causes sleep disturbances or if individuals who already have sleep problems appraise stress more negatively. This question has gained a growing interest among researchers and been widely discussed, yet the etiological relation remains unclear (Alvaro, Roberts et al. 2013). Results from studies on the bidirectionality between disturbed sleep and psychological health are equivocal (see for example (Jansson-Fröjmark and Lindblom 2010) (Morphy, Dunn et al. 2007) (Ohayon and Roth 2003) (Kaneita, Yokoyama et al. 2009). However, most evidence points to a bidirectional relation between stress and sleep, and with regard to study III, the longitudinal design provides more support to the hypothesis that stress lead to impaired sleep. As for study IV, the cross-sectional design can only demonstrate associations and provide a starting point, it does not show directionality or allow for causal interpretation.

Furthermore, there was a lack of vulnerable males in study I, the group with high sensitivity to stress was comprised of only women, which affected some of the measured variables that differed slightly when analyzing only women. Women in general, as for example the results of study IV shows, report a higher prevalence of stress, so it is very likely that a gender difference would have been evident had the sample included more male participants. Finally, a remark on generalizability, teachers are one of the most afflicted occupations in terms of stress (Hallsten, Bellaagh et al. 2002) in Sweden, and thus it is not clear whether the results of study I and II are representative of other occupational categories.

## **6.6 CONCLUSION**

Naturally occurring work stress of moderate intensity seems to have a moderately impairing effect on sleep, objectively shown as a decreased sleep efficiency and subjectively in feelings of not being fully restored and refreshed by sleep in the morning and higher levels of sleepiness. However, individuals with a pre-existing high vulnerability to stress-related sleep disturbances exhibited a more pronounced effect on sleep quality. They responded to the high stress work week with more microlevel sleep fragmentation and decreased REM sleep duration. The latter may possibly indicate an association of REM instability with stress-induced sleep reactivity, this is however speculative and the effects needs to be replicated and investigated further before any conclusions can be drawn. During the weekend, it appeared

that the impairment in sleep during the workweek was compensated through a longer sleep duration and more SWS. However, these effects will need to be reproduced in other studies. In chronically stressed individuals in the general population however, a reduced sleep duration was seen for both weekdays and days off, suggesting an impaired recovery ability.

Although daily variability in sleep quality seems quite sensitive to even modest variations in stress, a key factor in the day-to-day variation of sleep quality appears to be stress/worries at bedtime (rumination). The general population, particularly women and younger age-groups, attributed their disturbed sleep most often to stress. While the highest frequency of stress occurred in the 35-44 age group, peak stress disturbed sleep (most commonly manifested as lack of restoration) occurred in the age 45-54 years.

### **6.6.1 Practical implications**

Taken together, the results suggest that moderate, short-term, everyday stress has a limited impact on sleep quality and is probably not a plausible link to poor health for individuals with a low habitual vulnerability to stress-disturbed sleep. Thus, it is likely that stress activation needs to be extended, more intensive, and be present at bedtime in order to have a stronger impact on both objective and subjective indicators of sleep quality.

## **6.7 PERSONAL COMMENTARY**

So, is the day to day stress most of us experience quite regularly really that bad for our sleep? Well, judging by the results of the studies in this thesis the answer would be yes, although accompanied by a couple of ifs. Yes, if you are prone to high stress reactivity, if the stress lingers on and is still on your mind when it's time to go to sleep, and if there is no opportunity for recovery sleep in the days ahead. So if you are able to shake the stress off a couple of hours before bedtime, use the weekend nights for catching up on sleep, and if you are one of the lucky ones that are inherently resilient to stress, chances are that even if your perceived sleep quality is poor, your sleep may not be that disturbed during those stressful work periods. Provided of course it is just that, a limited time period.

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